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PARENTERAL BCG VACCINATION*

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B C G vaccine is commonly administered either enterally, that is, by mouth, or parenterally, that is, subcutaneously or intradermally. The enteral or oral method has been used in New York City since the beginning of 1927. The statistics concerning its value are favorable; still we have felt the need of the parenteral method. The advantages of this procedure compared to the oral are:

1. It can be given to patients of any age, provided they are free from tuberculosis and give a negative tuberculin reaction.

2. The control of the dosage is more exact than if we depend on absorption of the bacilli from the alimentary tract, from which only a small part of the orally given vaccine is absorbed and the other part excreted.

3. Those who believe that hypersensitiveness to tuberculin parallels immunity are more satisfied with the parenteral method because in 87 per cent of the cases the Mantoux reaction becomes positive, at least temporarily. Of our present seventy-four patients vaccinated longer than three months before this paper was written, sixty-four developed a strongly positive reaction to the standard amount of 0.2 mg. of old tuberculin and in ten the reaction remained negative to this routine dose; however, of the ten children three were not tested with a higher amount of old tuberculin than 0.2 mg.; of the seven who were tested, one gave a positive reaction to 2 mg., one a positive reaction to 5 mg., and one a positive reaction to 10 mg. In the other four the reaction remained negative.

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* The work here described was done in the Health Department of New York City through a generous grant from the Metropolitan Life Insurance Company. The B C G staff consists of Drs. William H. Park, Camille Kereszturi, Milton Levine and Peter Vogel. Margaret Sackett, R.N., our head nurse aided in the work. The institutions in which the work was actually carried out were Bellevue, Sea View, Fifth Avenue, Long Island College, Greenpoint, Staten Island and Harlem Hospitals. Dr. Charles Hendee Smith and Dr. Frederick Bartlett aided us particularly on their services. In obtaining the cases the Health Department and practically all the hospitals of the city were utilized. The statistics were closed on Jan. 15, 1931.

Considering the three factors mentioned and encouraged by the favorable reports from the literature, we started the parenteral B C G vaccination in May, 1929. Up to Jan. 15, 1931, we vaccinated seventy-eight patients parenterally. Some of them were vaccinated more than once, or were orally vaccinated the first time, so that the total number of vaccinations was ninety-one.

Only thirty-one children were vaccinated longer than one year before this writing; therefore we do not attempt to draw conclusions concerning the protective value of the vaccine administered parenterally, but limit ourselves to the study of the clinical consequences. As to the mortality rate, we shall state only that none of the seventy-eight parenterally vaccinated children has died of tuberculosis.

TABLE 1.—*Total Number of Parenteral Vaccinations and Age of the Children When Vaccinated*

	Primary Vaccination	Revaccination	Less Than 1 Year	1-2 Years	2-3 Years	More Than 3 Years
Subcutaneous	25	7	15	3	6	3
Intradermal	50	9	37	9	3	2
Total number	75	16	52	12	9	5

TABLE 2.—*Length of Time Elapsed Since Vaccination* *

	12 Months		6 Months		3 Months	
	More	Less	More	Less	More	Less
Subcutaneous	15	17	20	12	20	12
Intradermal	16	43	48	11	54	5
	31	60	68	23	74	17

* Sixteen of these patients were revaccinated.

SELECTION OF THE CASES

1. As a rule, we selected children only from families having cases of open tuberculosis. In our group of seventy-eight patients, seventy-three came from families with open tuberculosis and five from families with closed tuberculosis. This, however, does not mean actual exposure to tuberculosis in all cases, as the tuberculous member may still have been in a hospital or may have died before the exposure could occur.

2. In order to have patients of suitable age, we first took, with five exceptions, children up to 3 years of age. This group served the purpose of observing the reactions following vaccination. But in our recent study on the oral administration of B C G we observed that after the thirtieth month of life, the mortality of children from tuberculosis is very low both in the vaccinated and in the control groups. Therefore, in order to draw conclusions concerning the immunizing value of B C G, we decreased our age limit. For this reason we shall try to give the

parenteral B C G vaccine to younger children, i. e., to those within the first year of life. In the present study only two thirds of our patients were less than 12 months of age when vaccinated.

3. The child must give a negative Mantoux reaction to 0.2 and 2 mg. of old tuberculin previous to the vaccination. In the majority of cases this gives sufficient security to consider him free from tuberculosis. As we recently saw a considerable number of cases among the vaccinated babies who gave a negative reaction to 0.2 and 2 mg. of tuberculin but who reacted positively to 10 mg., we have decided that in the future we shall probably increase our tuberculin test dose to 10 mg. before B C G vaccination, not for elimination purposes, but because in case the reaction to amounts up to 2 mg. disappears after vaccination we can still resort to 10 mg. of old tuberculin before we consider the hypersensitiveness definitely abolished. When we made a statistical study of this problem, we found that in forty-two children reacting negatively to 0.2 mg. of old tuberculin we were able to demonstrate hypersensitiveness to tuberculin in sixteen, i. e., 36 per cent, if we increased the dose from 0.2 to 1, 2, 5 and 10 mg. Of course, all these patients were vaccinated with attenuated bacilli and were in a stage at which the positive tuberculin reaction is liable to disappear; i. e., this study was made within a limited number of months after parenteral B C G vaccination. In a group of naturally infected children we would not expect the reactions to the Mantoux test to vary to such an extent with the dosage of old tuberculin.

4. The physical examination, including roentgenograms of the chest, must not show any positive signs of tuberculosis.

5. From the time of vaccination until the tuberculin reaction turns positive, the children should be separated from any tuberculous person. We were unable to carry out this separation in fourteen of our seventy-eight cases. So far as we have seen, no harm was done which could have been attributed to the lack of separation. On the average, the positive Mantoux reactions did not appear sooner, but they remained longer among the exposed children than among those in the nonexposed group. Only those babies were counted who had been vaccinated more than three months. Fourteen other babies who lived in tuberculous surroundings after the Mantoux reaction turned positive had been vaccinated longer than twelve months.

COMPARATIVE STUDY OF SUBCUTANEOUS AND INTRADERMAL B C G VACCINATION

We used two types of parenteral B C G vaccination, namely, the subcutaneous and the intradermal. The results of the two methods are somewhat different; therefore, we shall describe our findings in a comparative way.

In the literature we found lower doses advocated for the subcutaneous method than for the intradermal one. Therefore, we used from 0.001 to 0.05 mg. of B C G subcutaneously, and from 0.003 to 0.15 mg. intradermally. Within these ranges we experimented with different doses in both the intradermal and subcutaneous groups for we wished to find the optimal dose, i. e., the amount of B C G vaccine that is harmless and that still gives hypersensitiveness to tuberculin for a sufficiently long period. We feel that we have not enough evidence as yet to call any of these doses the optimal one because, though none of the doses that we used was harmful, the hypersensitiveness to tuberculin in quite a number of cases did not last as long as we should have

TABLE 3.—*Comparative Study of Subcutaneous and Intradermal B C G Vaccinations, Disregarding Dosage* *

Method	No. Cases	Cold Abscess, per Cent	Papulo-macular Tuberculid, per Cent	Gland Enlargement, per Cent	Spleen Enlargement, per Cent	Positive Mantoux Reactions, per Cent	No. Cases	Positive Mantoux Reactions: Disappearing Within 12 Mo., per Cent	Positive Mantoux Reactions: Remaining Positive After 12 Mo., per Cent
Subcutaneous	20	60 (8 wks.)	..	60 (11 wks.)	30 (33 wks.)	90 (6½ wks.)	15	20 (33½ wks.)	50
Intradermal..	54	..	94 (2¾ wks.)	86 (9½ wks.)	35 (9½ wks.)	85 (4 wks.)	13	64 (26 wks.)	36
Total.....	74						28‡		

* Only those cases are included in which vaccination was done longer than three months before this paper was written.

† Only those cases are included as positive in which the positive reaction occurred to the routine dose with 0.2 mg. of tuberculin.

‡ This group includes only patients who were vaccinated longer than twelve months before (and were tested with a standard dose of 0.2 mg. of old tuberculin).

liked. In the future we shall be more inclined to increase our dosage than to decrease it.

From table 3 we can draw conclusions as to local lesions, gland and spleen enlargements, the first positive Mantoux tests and the disappearance of positive Mantoux reactions in both the subcutaneously and intradermally vaccinated groups.

Local Lesions.—In general, the larger the dose of B C G the sooner the local lesion appears. This is true only as an average because the individual reaction of each child—and perhaps the distribution of the vaccine in the tissue—disturbs the regularity of the relationship between the dose and the rapidity of the development of the local lesion (table 4).

Subcutaneous Group: In 40 per cent of the subcutaneous cases there was no local reaction whatsoever; we were unable to find the place where we injected the B C G vaccine. In 60 per cent of the cases a definite local reaction developed between the second and twenty-sixth week after the vaccine was given. The first sign was a small elastic

nodule deep in the subcutis. This became larger and larger, reaching more and more to the surface. After two months it became superficial and red. Soon after this stage, the abscess opened and we obtained thick greenish-yellow pus. The middle of the abscess usually sloughed away, the edges became elevated and in about two more months the abscess healed, leaving a scar from 5 to 10 mm. in diameter.

In one infant (M. I.) 0.001 mg. of B C G was injected subcutaneously. Forty-two weeks after the first vaccination this child had to be revaccinated, because its reaction to tuberculin had become negative. It is curious that, although she received the same dose on both occasions, she developed a cold abscess the first time but not the second time.

TABLE 4.—*Comparative Study of Subcutaneous and Intradermal B C G Vaccination According to Dosage*

Mg.	No. Cases	Cold Abscess, per Cent	Papulo-macular Tuberculids, per Cent	Gland Enlargement, per Cent	Spleen Enlargement, per Cent	First Positive Mantoux Reaction	Positive Mantoux Reactions: Disappearing Within 12 Mo., per Cent	Positive Mantoux Reactions: Remaining Positive After 12 Mo., per Cent
Subcutaneous								
0.001 0.002	10	40 (10 wks.)	0	60 (13 wks.)	50 (13 wks.)	9 wks.	80 (33 wks.)	20
0.0025 0.005 0.01 0.03 0.05	10	80 (7 wks.)	0	66 (4 wks.)	10 (42 wks.)	3½ wks.	0	100
Total	20							
Intradermal								
0.003 0.005 0.01 0.02 0.03 0.05	33	0	90 (2½ wks.)	78 (10 wks.)	29 (8 wks.)	8½ wks.	63 (23 wks.)	37
0.10 0.15	21	0	100 (2¾ wks.)	86 (8½ wks.)	23½ (13 wks.)	10½ wks.	66½ (35½ wks.)	64½
Total	74							

Sometimes we were able to observe around a discharging primary local reaction, miniature local lesions reminding us of tuberculids. This can be plainly seen in figure 1. These slight skin eruptions were observed mostly in cases in which the local lesion discharged. It is a question whether the eruptions developed by an endogenous, i. e., a lymphogenous progression of the bacilli, or by an exogenous extension through the discharge itself, which most probably contained numerous B C G.

Even when we decreased our original 0.05 mg. of B C G to a fiftieth of this dose the possibility of a cold abscess remained. These cold abscesses are not dangerous; they do not affect the general health of the child, but they are annoying on account of their chronicity and appearance.

It is interesting to note that after vaccination one of the children developed a chronic type of lesion, which had not broken down nineteen and a half months after vaccination. This is the second case in the series which reacted with a palpable but nonsuppurative lesion after a subcutaneous B C G vaccination.

We were anxious to learn the reason why some children develop a cold abscess after subcutaneous B C G administration whereas other children do not, even though the dosage is the same. We therefore studied our cases with respect to the following points: (1) whether the child is primarily vaccinated or revaccinated; (2) whether he is exposed to tuberculosis; (3) whether his subcutaneous tissue is well developed or scanty; (4) whether the vaccine is a fresh preparation or is nearing its expiration date, and (5) whether the same number of bacilli are given in a small or large amount of diluting fluid.

We are especially interested in discovering the answer to the fifth question, because last summer Dr. Calmette stated that if we diluted our B C G, as he does, in a greater amount of water, even though we employed the same number of bacilli as before, we would get a smaller percentage of cold abscesses. In the past we used from 0.1 to 0.3 cc. of diluent for one injection, whereas Calmette uses the B C G subcutaneously, diluted in from 1 to 2 cc. of fluid. We thought that the less we traumatized the tissues the better we could avoid the formation of a cold abscess. Calmette thought that the more we scattered the B C G bacilli in the subcutis the less chance there was to cause a tissue reaction. We vaccinated ten children, about three months before this writing, with 0.0025 mg. of B C G, using from 1 to 2 cc. of diluting fluid. So far nodules have developed in six and real cold abscesses in five.

Intradermal Group: We used from 3 to 150 times higher doses with the intradermal method than with the subcutaneous. In 94 per cent of the cases, we obtained local lesions, but these local lesions were entirely different from the ones produced by the subcutaneous method. The intradermal lesion appeared much more quickly, on the average between the second and third week, whereas the cold abscess of the subcutaneous vaccination occurred on the average during the eighth week after vaccination. The intradermal lesion was similar to a large skin tuberculid, a bluish-red, indurated papule with thin, shiny, wrinkled skin on the top. In some of the cases the papule never opened, but gradually became involuted in the course of from one to three months. In another group of cases a slight serous discharge was observed coming from the middle of the lesion. The discharge in the majority of cases was different from that of a cold abscess in quality and quantity; it was serous and very small in amount. Occasionally the center of the papule throughout an area from 1 to 5 mm. in diameter became necrotic and sloughed away. Whether the necrosis was due to the amount of bacilli

injected, the freshness of the growth, the concentration of the vaccine or the individual reaction of the child, we do not know as yet. It seems to us that the depth of the injection has a great significance. If we do not succeed in giving the vaccine quite superficially, we run a greater risk of necrosis formation. Concerning the significance of necrosis of the local lesions in general, we do not know enough to generalize. Wallgren,[1] in his pioneer article on parenteral B C G vaccination, said: "I have never seen tuberculin allergy develop in those cases that did not show any demonstrable reaction." He used from 0.1 to 3 mg. of old tuberculin for his tuberculin reactions and called a test positive if it was more than 10 mm. in diameter and was red and infiltrated on the third day after it was given. We do not agree with him entirely, but that may be only because our definition of a positive test is somewhat different. We call a tuberculin test positive if it shows more than a 5 mm. reaction two days after it is done. We may include an occasional pseudoreaction as a true one. We have the impression that in both subcutaneous and intradermal cases with a local lesion the patients had a more strongly positive Mantoux reaction and tended to keep their hypersensitiveness to tuberculin longer than those who showed no sign of a local lesion. But we saw quite a number of cases in which the patients showed no local lesion and still developed a positive Mantoux reaction.

From a cosmetic point of view, the intradermal local lesion is preferable to the subcutaneous one.

Gland Enlargements.—Subcutaneous Group: We give the vaccine in the lateral part of the left thigh between the middle and lower third. In 60 per cent of the subcutaneous cases the lymph nodes in the groin on the same side as the injection became enlarged in an average time of eleven weeks. In only one case was there suppuration, but this patient received 0.05 mg., which for subcutaneous use in an extremely high dose. In the majority of cases the lymph node enlargement was very slight and became definite after the abscess opened and secondary infection took place. The length of time during which the lymph node enlargement was noticeable varied from a few weeks to a few months.[2]

Intradermal Group: The lymph node enlargement occurred somewhat more frequently in the intradermal than in the subcutaneous group; that is, it occurred in about 86 per cent of the cases and in a slightly shorter average time, in about nine and one-half weeks. In most of the cases the lymph node enlargement was also slight, the nodes being

1. Wallgren, A.: Intradermal Vaccinations with B C G Virus, J. A. M. A. **91**:1876 (Dec. 15) 1929.

2. Since this article was submitted for publication, discharging lymph nodes were observed in the groin in two other children.

merely a little more palpable on one side than on the other; but in a small number of cases the lymph glands were markedly enlarged, and in two instances pus formation occurred.

Spleen Enlargements.—Subcutaneous Cases: In the twenty subcutaneous cases we observed not more than six patients with enlargement of the spleen. The average time elapsing before we noticed the spleen enlargement was thirty-three weeks. This date was so long subsequent to the actual vaccination that it is questionable that the splenic enlargements and B C G vaccination were in causal relationship.

Intradermal Cases: In the intradermal group the splenic enlargement occurred in 35 per cent of the cases in an average time of nine and one-half weeks. As a great many other conditions may have influenced the size of the spleen, it is not certain that our study of the spleen will lead us to any specific conclusions.

Positive Mantoux Test.—As we mentioned before, in 10 per cent of the subcutaneously and in 15 per cent of the intradermally vaccinated patients no hypersensitiveness developed to tuberculin; at least we could not demonstrate it with the routine dose of 0.2 mg. of old tuberculin. But with the exception of the percentages noted, the cases showed a definitely positive reaction in an average time of six and one-half weeks in the subcutaneous and four weeks in the intradermal group. As the patients vaccinated subcutaneously received a smaller dose than those vaccinated intradermally, they probably therefore developed hypersensitiveness to tuberculin more slowly.

The disappearance of a positive reaction is gradual. After failure to get a reaction with 0.2 mg. of tuberculin we were able to produce for a time a positive reaction if we sufficiently increased the amount of tuberculin used in the test. We never went higher than 10 mg. of old tuberculin. The transition is a few months in duration.

Fifty per cent of our subcutaneously vaccinated patients maintained their hypersensitiveness to tuberculin for more than twelve months and some of them for as long as twenty months or more. The other 50 per cent gave a negative reaction to tuberculin within twelve months, in an average time of thirty-three and one-half weeks.

In the intradermal group 64 per cent of the patients lost their positive tuberculin reaction in an average time of twenty-six weeks. The remaining 36 per cent had a positive tuberculin reaction twelve or more months after vaccination. Figure 5 shows the percentage of the children who gave a positive tuberculin test in various months after B C G vaccination. The standard Mantoux test dose was 0.2 mg. The figures were determined every month. When no test was made during the month, if that made the previous month and the next tests were positive, we considered the hypothetic test in the month in question also positive. On

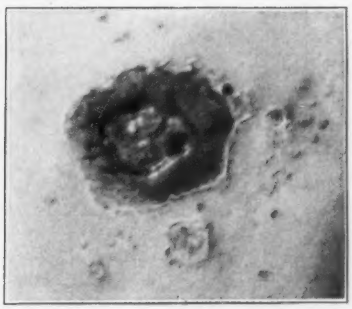

Fig. 1.—Site of vaccination in D. L., five months after 0.002 mg. of B C G was given subcutaneously.

Fig. 2.—The completely healed local lesion shown in figure 1, two and a half years after vaccination. This is one of the largest scars that we ever obtained.

Fig. 3.—Site of vaccination in C. B., one and a half months after intradermal vaccination with 0.05 mg. of B C G.

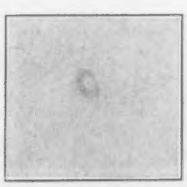

Fig. 4.—The local lesion shown in figure 3, completely healed, one year and two months after vaccination.

the other hand, between two negative tests we also took the liberty to substitute a hypothetic negative test. Between a negative and a positive test we left the space empty.

From figure 5 it is obvious that after parenteral B C G vaccination the frequency of positive tuberculin tests rises for about three or four months, and from this time on, it drops. The subcutaneous method gives somewhat higher percentages.

The disappearing positive Mantoux tests are important observations; they answer the very much discussed question whether or not a positive

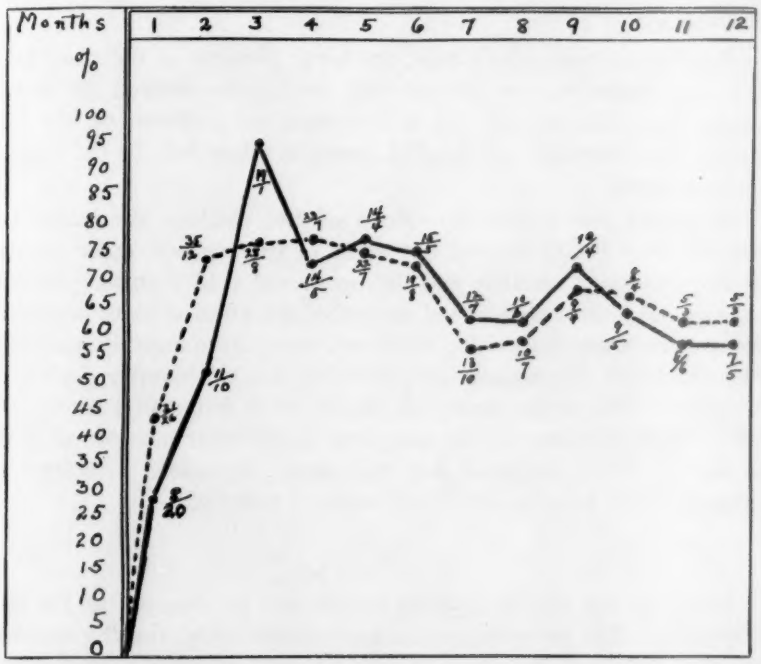

Fig. 5.—Frequency of positive Mantoux tests after B C G vaccination (with a standard dose of 0.2 mg. of old tuberculin). The solid line indicates the subcutaneous method and the dotted line the intradermal method.

tuberculin reaction accompanies a person through his entire life or whether it is liable to change. Of course we must realize that our disappearing positive reactions were provoked by a small number of slightly virulent bovine type of tubercle bacilli, whereas a natural infection is produced usually by a greater number and a more virulent type of tubercle bacilli. However, a change in the hypersensitiveness to tuberculin can also occur under natural conditions for we have seen changing Mantoux reactions among our control babies, i. e., children who were not vaccinated and in whom the positive Mantoux reaction was due to natural infection.

We think that the disappearance of the hypersensitiveness in our vaccinated patients after such a relatively short time as from twenty-six to thirty-three and one-half weeks indicates possibly that our dosage is too small. We should either use larger doses or revaccinate the children more frequently.

Revaccinations.—Up to the present, we have revaccinated sixteen children. Three of them were orally vaccinated previously; nine belonged to the intradermal group, and four to the subcutaneous group. They have not been vaccinated long enough to determine whether their reactions will be similar to those of the primarily vaccinated group or not.

Roentgenograms.—As a rule, the x-ray pictures of the chest taken after a subcutaneous or intradermal vaccination showed no definite change from the normal. In a few cases an increase of the hilus shadow was observed. A detailed roentgen study will be the topic of a future paper.

Morbidity and Mortality.—None of the children vaccinated parenterally with B C G showed any signs of tuberculosis, other than the positive Mantoux reaction and the occasional cold abscess. No temperature, no loss of weight and no pathologic physical signs suggesting tuberculosis were observed. However, one subcutaneously vaccinated baby developed phlyctenular conjunctivitis five weeks after the vaccine was given. This ocular condition cleared up in less than a week. Of seventy-eight children we lost one, three weeks after intradermal B C G vaccination. The diagnosis was aspiration pneumonia. Autopsy was performed and failed to show any signs of tuberculosis.

SUMMARY

Many of the aforementioned figures will be changed as the work progresses. The percentages are approximate only, for the following reasons:

1. The children were of different ages.

2. They were vaccinated with doses of different sizes. We already know that if we alter the dosage the percentage of children developing the tuberculin reaction will be changed. This is shown in table 4.

3. The vaccinated and revaccinated children are not grouped separately.

4. Slight attention only has been paid in this paper to the extent of the exposure to tuberculosis as an influencing factor in the development and persistence of the tuberculin reaction.

CONCLUSIONS

1. Intradermal B C G vaccination is superior to the subcutaneous type, as used by us, because if the technic is correct no cold abscess

develops. On the other hand, hypersensitiveness to tuberculin occurs a little more frequently and lasts somewhat longer when we employ the subcutaneous method.

2. In 87 per cent of our parenterally vaccinated patients hypersensitiveness to tuberculin developed either temporarily or for a longer period.

3. The use of both the subcutaneous and the intradermal methods of B C G vaccination has been harmless.

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THE VALUE OF AN INCREASED SUPPLY OF VITAMIN B_1 AND IRON IN THE DIET OF CHILDREN *

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During the past five years it has been conclusively demonstrated that the complex formerly known as vitamin B consists of at least two separate and distinct vitamins; the antineuritic or thermolabile factor designated as vitamin B or B_1, and the pellagra-preventing or thermostabile factor designated as vitamin G or B_2. Recent studies of these two vitamins indicate that the antineuritic factor is not so abundant or so widely distributed in foods as was formerly supposed. The most concentrated sources of these vitamins are yeast and the germ of cereal grains. There are only minute amounts in milk, meat, fruits and vegetables, and practically none in the highly milled products such as white flour and farina, in which the germ and bran are discarded. When it is realized that highly milled cereal products constitute over 30 per cent of the calories in the average diet,[1] it is obvious that care must be taken with the selection of the remaining portion of the diet in order to supply the optimum amount of the antineuritic vitamin.

In animals, one of the striking symptoms produced by a lack of vitamin B_1 is a loss of appetite. After from five to ten days, rats deprived of this vitamin cease gaining in weight and die in the course of from four to five weeks. A diminished tone of the whole intestinal tract can readily be observed. Fletcher and Graham [2] have shown that the dilated colons encountered in many rheumatic adults can be brought back to normal size by the administration of wheat germ and a reduction of the amount of carbohydrate in the diet. Hoobler,[3] Dennett,[4] Bartlett [5] and others have suggested that a lack of this vitamin may be an impor-

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* From the Nutritional Research Laboratories of the Department of Paediatrics, University of Toronto, and the Hospital for Sick Children, under the direction of Alan Brown, M.B.

1. Editorial: The Place of Wheat in the Diet, J. A. M. A. **93**:119 (July 13) 1929.

2. Fletcher, A. A., and Graham, D.: Am. J. M. Sc. **179**:91, 1930.

3. Hoobler, B. R.: Symptomatology of Vitamin B Deficiency in Infants, J. A. M. A. **91**:307 (Aug. 4) 1928.

4. Dennett, R. H.: Routine Use of the Vitamin B Factor in Infant Feeding, J. A. M. A. **92**:769 (March 9) 1929

5. Bartlett, W. M.: An Analysis of Anorexia, Am. J. Dis. Child. **35**:26 (Jan.) 1928.

tant factor in anorexia in certain infants. Also, resistance against infection is markedly reduced.[6] Recently, Morgan and Barry have demonstrated in a striking manner the effect of feeding wheat germ to undernourished children.[7] These investigators took two groups of underweight children from 11 to 13 years of age and compared them as to growth in weight, height and certain other physical measurements over three periods totaling thirty weeks. Each child in the wheat germ group in each period was required to include in the noon meal 3 ounces of rolls made with 50 per cent wheat germ and 50 per cent white flour, thus ingesting a total of 5 ounces of wheat germ per week. The control group took the usual white flour rolls. The weight increases in each of the wheat germ periods were about three times as great as in the control periods. The height increases were significantly greater in two of the wheat germ periods than in the corresponding control groups.

In view of the results reported by Morgan and Barry,[7] it was thought that it would be of interest to study the weight increases of a number of children fed a special cereal mixture[8] composed of farina 53 per cent, oatmeal 18 per cent, corn meal 10 per cent, wheat germ 15 per cent, bone meal 2 per cent, dried brewers' yeast 1 per cent and alfalfa leaf meal 1 per cent. During the past year, practically all the children in the Hospital for Sick Children have been fed this cereal. In addition to supplying energy, it furnishes vitamins in liberal amounts, including the antineuritic vitamin derived from wheat germ and the yeast. The children observed were in a preventorium. They were essentially normal children of about average weight for age and height. In this rather important respect, this investigation differs from that reported by Morgan and Barry,[7] in which the children observed were all underweight. Twenty-one children in all, consisting of fifteen boys and six girls, were observed over a period of twenty weeks. They ranged in age from 6 to 13 years. The majority of the children had been in the preventorium for more than one and one-fourth months before the observations were started, and during this time they had been on the regular diet, which included milk, meat, eggs, vegetables and fruit. A diet of this nature is usually considered to furnish in adequate amounts the vitamins necessary for optimal development.

The children were divided into two groups, numbers 1 to 11 and 12 to 21. Numbers 1 to 11 were given each day for ten weeks 4 ounces

6. Ross, J. R., and Robertson, E. C.: The Effect of Vitamin B Complex on the Resistance of Rats to Enteritidis Infection, Am. J. Dis. Child., to be published.

7. Morgan, A. F., and Barry, M. M.: Underweight Children: Increased Growth Secured Through the Use of Wheat Germ, Am. J. Dis. Child. **39**:935 (May) 1930.

8. Tisdall, F. F.; Drake, T. G. H., and Brown, A.: A New Cereal Mixture Containing Vitamins and Mineral Elements, Am. J. Dis. Child. **40**:791 (Oct.) 1930.

of the special cereal mixture. This furnished in the course of one week 4.2 ounces of wheat germ and 0.28 ounce of dried yeast. Two ounces of this cereal was given for breakfast, and a muffin containing 1 ounce of the cereal was given at both dinner and supper. The remainder of the diet consisted of the routine food offered by the institution.

TABLE 1.—*Increase in Weight of Children Numbers 1 to 11, Receiving Special Cereal During First Ten Weeks*

Number of Child	Age, Years	Weight, Pounds	Deviation from Average Weight for Age and Height,* Pounds	Expected Gain During Ten Weeks,† Pounds	Actual Gain, Pounds
1	6	44.50	0	0.6	3.25
2	11	59.75	0	1.2	1.25
3	11	72.00	+ 7	1.2	4.75
4	11	63.50	0	1.2	5.50
6	9	57.25	— 4	1.2	3.75
7	10	60.25	+ 1	1.2	2.25
8	8	47.50	0	1.0	2.50
9	12	64.25	0	2.0	12.25
10	11	62.75	+ 1	1.6	5.75
11	10	62.50	+ 2	1.6	4.00
Average	10	.....	+ 0.18	1.27	4.54

Rate of gain 3.57 times the expected rate

* In this and the succeeding tables, the average weight for age and height is based on statistics obtained from 59,291 presumably healthy school children in Toronto by the Toronto Department of Public Health.

† In this and the succeeding tables, the expected gain in weight is based on the statistics compiled by the Toronto Department of Health.

TABLE 2.—*Increase in Weight of Children Numbers 1 to 11, Receiving Ordinary Cereals During Second Ten Weeks*

Number of Child	Age, Years	Weight, Pounds	Deviation from Average Weight for Age and Height, Pounds	Expected Gain During Ten Weeks, Pounds	Actual Gain, Pounds
1	6	47.75	+ 3	0.6	1.25
2	11	61.00	+ 1	1.2	0.50
3	11	76.75	+11	1.2	3.00
4	11	69.00	+ 6	1.2	1.00
5	11	74.00	0	1.2	2.50
6	9	61.00	0	1.2	0.50
7	10	62.50	+ 3	1.2	—0.25
8	8	50.50	+ 2	1.0	1.25
9	12	76.50	+11	2.0	4.00
10	11	68.50	+ 7	1.6	—1.00
11	10	66.50	+ 6	1.6	1.75
Average	10	.....	+ 4.5	1.27	1.25

Rate of gain is just at the expected rate

Numbers 12 to 21 acted as a control group for the first ten weeks. They received 2 ounces of ordinary cereal (farina, oatmeal, corn meal and cut wheat) for breakfast and two muffins a day, each containing 1 ounce of white flour, which is essentially the same as farina. The caloric values of the special cereal mixture and the ordinary cereals are the same. At the end of ten weeks the groups were changed, numbers 1 to 11 now receiving for the second ten weeks ordinary cereals, and numbers

12 to 21 receiving the special cereal mixture. One nurse was in charge of these children at meal hours and saw that the cereal and muffins were consumed by each child each day. They were then allowed to eat as much of the remaining food as they desired. The results of the weight increases are given in tables 1 to 4 and in the accompanying chart.

TABLE 3.—*Increase in Weight of Children Numbers 12 to 21, Receiving Ordinary Cereals During First Ten Weeks*

Number of Child	Age, Years	Weight, Pounds	Deviation from Average Weight for Age and Height, Pounds	Expected Gain During Ten Weeks, Pounds	Actual Gain, Pounds
12	7	52.25	+ 4	1.0	0.50
13	6	46.00	+ 2	0.6	1.75
14	7	56.00	+ 4	1.0	1.25
15	8	50.25	+ 2	1.0	1.25
16	9	53.50	— 3	1.2	3.50
17	7	51.00	+ 7	1.0	—0.25
18	8	50.50	+ 2	1.0	2.75
19	13	93.50	+10	1.8	1.50
20	10	63.50	+ 3	1.2	0.75
21	8	50.75	0	1.0	—0.25
Average	8.4	.....	+ 3.1	1.08	1.27

Rate of gain 1.17 times the expected rate

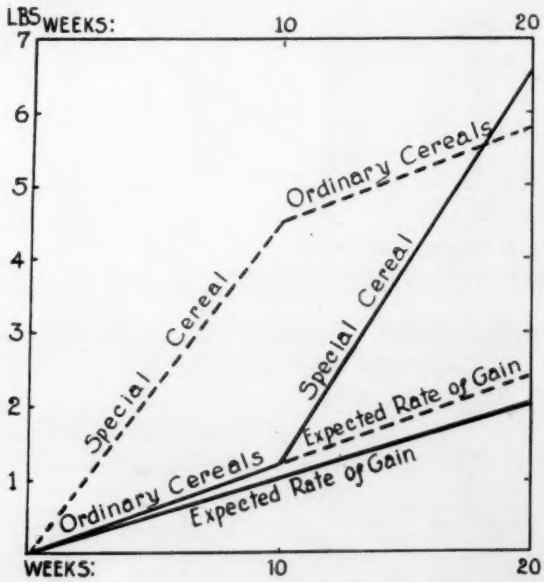
TABLE 4.—*Increase in Weight of Children Numbers 12 to 21, Receiving Special Cereal During Second Ten Weeks*

Number of Child	Age, Years	Weight, Pounds	Deviation from Average Weight for Age and Height, Pounds	Expected Gain During Ten Weeks, Pounds	Actual Gain, Pounds
12	7	52.75	+ 4	1.0	3.25
13	6	47.75	+ 3	0.6	3.75
14	7	57.25	+ 5	1.0	4.25
15	8	51.50	+ 3	1.0	3.25
16	9	57.00	+ 1	1.2	5.75
17	7	50.75	+ 6	1.0	3.25
18	8	53.25	+ 5	1.0	3.25
19	13	95.00	+11.5	1.8	10.00
20	10	64.25	+ 0	1.2	4.75
21	8	50.50	+ 0	1.0	6.25
Average	8.4	.....	3.8	1.08	5.27

Rate of gain 4.88 times the expected rate

It is evident from the results given in tables 1 to 4 that the children gained much more rapidly when fed the special cereal than when fed ordinary cereals. It should be noted that at the beginning of the first ten week period, the children fed ordinary cereals were an average of 4.5 pounds above the expected weight for age and height, while those fed the special cereal were only 0.18 pound above the expected weight. However, during the second ten week period the variation from the expected weight of the two groups is about the same (3.1 pounds as compared with 3.8 pounds).

Rosenberg [9] has reported the effect of feeding twenty-five children a diet consisting of a quart of certified milk daily, a variety of nuts, whole grain cereal products three times a day and fresh fruits and vegetables twice a day, with meat and eggs excluded. The increase in weight in this experimental group at the conclusion of a six months' period was 32 per cent greater than that in a control group on a representative American diet. Rosenberg stressed the importance of the vitamin B complex and the preponderance of base-forming over acid-forming elements in this diet. Although the special cereal mixture used in the



Comparison of the increase in weight with the special and the ordinary cereals.

present investigation is base-forming, being a rich source of many of the essential minerals as well as containing a liberal amount of vitamins A, B_1, B_2 and E, we think, in view of the results obtained by Morgan and Barry,[7] that the striking rate of gain in weight of our children is probably the result of the vitamin B_1 furnished by the wheat germ and yeast.

These results raise the question as to whether the average child today is receiving an amount of vitamin B_1 sufficient to produce the optimal rate of growth.

9. Rosenberg, L. C.: Malnutrition in Children: An Attempt at Standardization of a Dietary, Am. J. Dis. Child. **41**:303 (Feb.) 1931.

HEMOGLOBIN DETERMINATIONS

McKay,[10] in 1926, found in a dietary study of the preschool child that for boys the average daily intake of iron was 7 mg. and for girls the average intake was 6.99 mg. Rose and her associates,[11] in their recent publication on the iron requirement in early childhood, found that their subject took 4.64 mg. of iron daily. With this intake, they found that the average daily balance of iron for the nine days was negative to the extent of 1.10 mg. Thus the minimum requirement was about 5.70 mg. of iron. In order to provide some surplus for growth, they recommended an iron intake 50 per cent greater than this minimum figure, or a total daily intake of about 8.50 mg. of iron. In view of the fact that each ounce of the special cereal mixture used in the present investigation supplies no less than 6.8 mg. of iron in contradistinction to other cereals, such as farina, which supplies only 0.3 mg. of iron, it was thought that it would be of interest to follow any changes in the hemoglobin concentration in the children under observation. The special cereal mixture also contains an adequate supply of copper.

The hemoglobin determinations were made on the blood by the Newcomer method. At the beginning of the investigation numbers 1 to 11, fed the special cereal mixture, had an average hemoglobin of 9.8 Gm. per hundred cubic centimeters of blood. During the next ten weeks, they made an average gain of 1.5 Gm. of hemoglobin per hundred cubic centimeters of blood, the average hemoglobin being 11.3 Gm. This group was then changed to ordinary cereals. During the next ten weeks while on ordinary cereals, their average loss was 1.2 Gm. of hemoglobin per hundred cubic centimeters of blood, the hemoglobin finally being 10.1 Gm. At the beginning of the investigation, numbers 12 to 21 started with an average hemoglobin of 9.3 Gm. per hundred cubic centimeters of blood. During the next ten weeks, while fed ordinary cereals, they made an average gain of 1.2 Gm. per hundred cubic centimeters of blood, the average hemoglobin being 10.5 Gm. This group was then changed to the special cereal mixture. During the next ten weeks, while on the special cereal mixture, the hemoglobin still improved, so that there was a further gain of 0.7 Gm. of hemoglobin per hundred cubic centimeters of blood, the average hemoglobin being 11.2 Gm.

It is difficult to evaluate these results owing to the differences in the hemoglobin concentrations of the two groups at the beginning of the periods under observation. However, at the conclusion of the periods during which the children were fed the special cereal mixture, numbers

10. McKay, H.: Ohio Agric. Exper. Sta. Bull., 1926, p. 400.

11. Rose, M. S.; Vahlteich, McC.; Bloomfield, E., and Robb, E. M.: J. Nutrition **3**:229 (Nov.) 1930.

1 to 11 had an average hemoglobin of 11.3 Gm. per hundred cubic centimeters of blood, and numbers 12 to 21 an average of 11.2 Gm. In contrast to these figures, at the conclusion of the periods during which the children were fed ordinary cereals, numbers 1 to 11 had an average hemoglobin of 10.1 Gm. per hundred cubic centimeters of blood, and numbers 12 to 21 an average of 10.5 Gm. Also, the average gain in hemoglobin concentration while on the special cereal mixture was 1.5 Gm. per hundred cubic centimeters of blood for the first group and 0.7 Gm. for the second group, or an average for the two groups of 1.1 Gm. On the ordinary cereal, the first group lost an average of 1.2 Gm. of hemoglobin per hundred cubic centimeters of blood, while the second group gained 1.2 Gm. This makes an average gain in hemoglobin concentration for the two groups while on ordinary cereal of exactly nothing.

SUMMARY

1. The daily administration of 4 ounces of a special cereal mixture composed of farina 53 per cent, oatmeal 18 per cent, corn meal 10 per cent, wheat germ 15 per cent, bone meal 2 per cent, dried brewers' yeast 1 per cent and alfalfa leaf meal 1 per cent, thereby supplying in liberal amounts calcium, phosphorus, iron, copper and vitamins A, B_1, B_2 and E in the diet of eleven children of approximately normal weight, over a period of ten weeks, resulted in a weight increase at 3.57 times the expected rate of gain. A control group of ten children fed 4 ounces of ordinary cereals in the daily diet gained at 1.17 times the expected rate.

2. For a second ten week period the groups were reversed, and the control group now received the special cereal mixture. The rate of gain of these children was 4.84 times the expected rate. The new control group, formerly on the special cereal mixture and now receiving ordinary cereals, gained at just the expected rate.

3. These results, in conjunction with those reported by Morgan and Barry,[7] raise the question as to whether the average child today is receiving an amount of vitamin B_1 (the antineuritic vitamin) sufficient to produce the optimal rate of growth.

4. The average hemoglobin concentration at the conclusion of the periods during which the children were fed the special cereal mixture was 11.3 Gm. per hundred cubic centimeters of blood for numbers 1 to 11, and 11.2 Gm. for numbers 12 to 21.

5. The average hemoglobin concentration at the conclusion of the periods during which the children were fed ordinary cereals was 10.1 Gm. per hundred cubic centimeters of blood for numbers 1 to 11, and 10.5 Gm. for numbers 12 to 21.

6. It would appear that the high iron content of the special cereal mixture is of value in increasing the hemoglobin content of children.

THE MECHANISM OF ANEMIA ASSOCIATED WITH INFECTION IN INFANCY AND IN CHILDHOOD*

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Anemia is a common manifestation of infectious invasion in infancy and childhood. It appears abruptly with the sudden onset of an acute infectious disease like diphtheria or develops gradually as a result of chronic infection in the child's body. Anemia may appear as the first striking clinical expression of a chronic focus of infection like sinusitis. While anemia as a systemic injury by infection is not always discernible, its correction is indispensable in effective recovery. Clinical observations of the varied responses on the part of infants and children to therapeutic procedures instituted in the course of infection or during convalescence have led us to raise a number of questions regarding the anemias associated with infection. How do various infections actually produce anemia? Is the severity of infection directly related to the resulting degree of anemia? Does infection injure the blood-forming tissues or their products in the circulating blood? Are the anemias associated with infection amenable to treatment in the course of infection? What relation has anemia associated with infection to the rate of recovery? These, among other questions, arise again and again in the course of clinical observations of infants and children suffering from some infectious disease.

Anemia associated with infection usually results from either the diminished production of erythrocytes, the so-called aplastic anemia, or from increased destruction of circulating erythrocytes, the so-called hemolytic anemia. Certain infections, on the other hand, may actually be productive of hemorrhage to the extent of being the determining factor in the development of the resulting anemia. These types of anemia occurring with infection either exist alone as well defined entities or as combinations of all three mechanisms. In fact all forms of anemia occur, from that due purely to the absence of blood formation to that due to increased blood destruction, and between these extremes are observed instances in which both factors play a part and in which one factor may be much more in evidence than the other. A systemic study

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* From the Department of Pediatrics, the Fifth Avenue Hospital.

of the infectious diseases, both acute and chronic, in children made from the standpoint of the associated anemia was carried out to determine the factors operative in depressing the hemoglobin and red cells of the circulating blood. Such determinations are made possible by the fact that the reticulated cell count is directly related to the level of bone marrow function, and the icteric index parallels the amount of hemoglobin destruction in the circulating blood. Quantitative determinations of these and other blood components involved in the hematogenic and hemolytic balance offer a first approach to an understanding of the anemic mechanism.

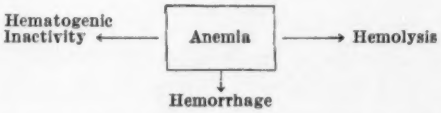


Fig. 1.—Three mechanisms in anemia associated with infection.

THE NORMAL HEMATOPOIETIC EQUILIBRIUM IN CHILDHOOD

The hematopoietic system is a very labile mechanism in infancy and childhood. The younger the infant, the more unstable the blood regenerative system, to the extent that it may react in a very bizarre manner to a stimulus. But this is characteristic of all other systems of the child's body. The normal range of blood values varies considerably during the first year of life. Though the factors productive of anemia are the same in infants as in adults, the violence of the reaction in children may produce severe grades of anemias, while in adults the fall in hemoglobin or red cells may be so slight as to be of no clinical significance. The variability of the juvenile reaction to a pathologic process requires a more critical approach to its evaluation and subsequent solution so far as it affects the blood picture.

The bone marrow is a very plastic tissue consisting of fat cells, a vascular structure and blood-forming islets supported by a reticulum. The arterioles are thick-walled, while the sinuses have thin walls made up of a single layer of endothelial cells. The fat cells and erythrogenic islets lie between these venus sinuses. The erythrocytes grow in definite groups in the reticulum of the bone marrow. The nucleated cells and those showing mytosis are arranged centrally in definite grouping within the bone marrow. The nearer the cells are to the periphery, the more mature do they appear. The adult cells thus lie in contact with the thin endothelial cells that constitute the walls of the venous sinuses. They contain blood at very low pressure, and so it is into these yielding structures that adult red cells are forced into circulation by virtue of internal growth gradients. Red cells are constantly pro-

duced in the erythrogenic islets without affecting the rate of disintegration of the red cells in the peripheral circulation.

Early in the development of the embryo, erythrocytes are the first of the blood cells to be differentiated within the endothelial lining of the vessels. At first the primitive erythroblasts are megaloblastic, and later when red cell formation becomes extravascular, normoblasts give way to megaloblasts. The blood-forming tissues are distributed at first throughout the embryo, gradually becoming concentrated within the liver, the spleen and finally within the bone marrow, all the bones participating at birth. Throughout autogenic development a continuous

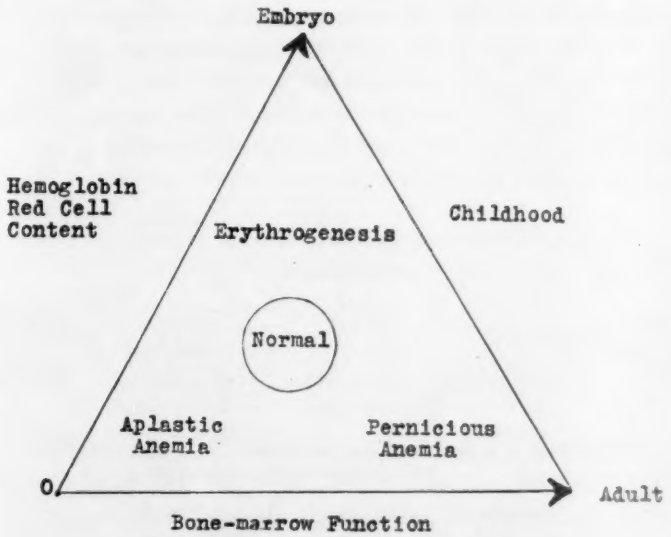


Fig. 2.—The erythrogenic triangle.

hematopoietic metamorphosis occurs as a result of the rapidly increasing blood demand. It does not cease at birth, since considerable lability of the hematopoietic system persists throughout postnatal life, though to a lesser degree than during fetal development. In the new-born the islets showing blood-forming activity are found not only in the red bone marrow but also in the liver, spleen and lymphatic tissue. But several months after birth, the erythrogenic function becomes limited to the red bone marrow of all bones, where it remains localized until adolescence. As blood demand decreases during adult years, the formerly active bone marrow of the long bones is replaced by fat. Then the erythrogenic function becomes limited to the flat bones, the spongy bones, especially the ribs, the vertebrae, the skull and the heads of the long bones. Their marrow remains proliferative for adjustment to a

stable equilibrium stimulated merely by the demand set up by the everyday wear and tear of destruction.

Transition of Erythrogenic Islets with Growth

Embryo	Infancy	Childhood	Adult
Entire structure	Red bone marrow Liver Spleen Lymphatics	Red bone marrow of all bones	Flat bones Spongy bones Heads of long bones

The normal blood picture consists of circulating matured erythrocytes of different ages. They are highly differentiated cells containing neither nucleus nor any definite internal structure. The earliest forms of normal red blood cells are stored in the hematopoietic organs. The release of new mature cells from these blood-forming organs to displace the physiologically worn out cells is referred to as regeneration, the mechanism of which is as yet unknown. The presence of immature red blood cells in the circulating blood is an indication of an accumulation of new cells in response to some strong stimulus. These rela-

TABLE 1.—*The Normal Compared with the Anemic Mechanism*

	Mechanism	
System	Normal	Anemic
Erythropoietic	Production	Diminution
Circulatory	Delivery	Destruction
Tissues	Function	Hemorrhage

tively young cells are believed to be rushed into the circulation before maturation to meet urgent demands for cells. The immaturity may be recognized by cytoplasmic changes in the red cells brought about by staining methods.

Normal variations in hemoglobin and red cells in infancy and childhood have been found by various workers to show considerable differences. All authorities have agreed that at birth the amount of hemoglobin is high, the average being about 110 per cent. After birth, this falls, reaching the value of about 80 per cent during the third week, and remaining at approximately this level until about the second year of life. The subsequent slight rise tends toward the level of adult values. But the hemoglobin may be brought to saturation in infancy by the administration of iron. The changes in the red cell count during the first days of life are comparable to the hemoglobin content. The blood taken from the umbilical cord at birth gives higher values than the accepted average of about 5,500,000 for the new-born infant. After the second week, the count remains at about the 5,000,000 level for both sexes. The infant's transition to more adequate oxygen supply diminishes the total red cell concentration, with a production of hemolysis and physiologic jaundice of varying degrees. As a result of the

new environmental stimulus, many cells are irregular in shape and size and occasionally nucleated. The resistance to hypotonic saline solution is invariably decreased.

THE NATURE OF BLOOD DESTRUCTION

The average life of the red cell under normal conditions is between twenty and thirty days. This necessitates the daily removal from the circulation of a mass of red cells corresponding to between 25 and 100 cc. of blood in children. Rous [1] has demonstrated that as a result of the buffeting the red cells encounter in the circulation they are eventually broken up, but without the liberation of the hemoglobin into the plasma. The resulting cell fragments are filtered out largely into the spleen, where they are engulfed by macrophages, thus completing the process of disintegration. The reticulo-endothelial cells of the liver, the lymph glands and even the bone marrow participate in this removal of the red cells from the circulation. The rate of normal utilization of

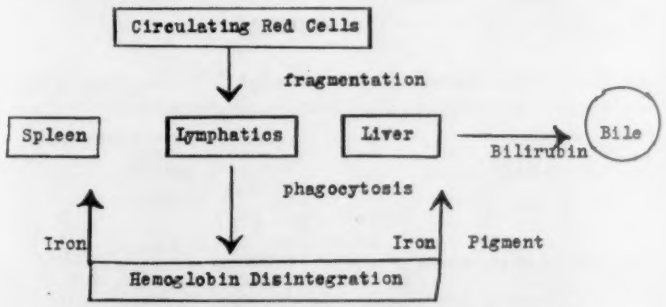


Fig. 3.—The physiologic destruction of erythrocytes.

red cells, i. e., physiologic red cell destruction, has been shown by Brown [2] to be dependent on the degree of muscular activity. The hemoglobin of the disintegrated cells is decomposed, and the iron strained in the spleen and liver for the resynthesis of fresh hemoglobin. The remaining constituent of the hemoglobin molecules is converted into bilirubin by the reticulo-endothelial cells. It is then carried by the plasma to the liver where it is taken up by the glandular cells and excreted into the bile.

Hemolytic anemias characterized by direct toxic injury to the red cells show microscopically that the damaged cells are removed from the circulation before hemoglobin is liberated. The reticulo-endothelial cells, the spleen and other organs become overactive in the physiologic process of red cell destruction. Part of the pigment liberated on disintegration of the hemoglobin molecule is transformed in these tissues into bili-

1. Rous, P.: Physiol. Rev. **3**:75, 1923.
2. Brown, A. L.: J. Exper. Med. **36**:481, 1922.

rubin. It circulates in the blood in protein combination, and is liberated and excreted by the liver. The bacteria in the intestinal tract further transform it into urobilinogen, which is reabsorbed into the portal circulation. It is again absorbed by the liver, reconverted into bilirubin and excreted into the bile. Abnormal destruction of red blood cells will therefore be reflected in the excretion of bilirubin and in the production of urobilinogen, provided liver function is not greatly impaired and there is no biliary obstruction. If the rate of urobilinogen formation exceeds that at which it can be removed from the portal circulation by the liver, it will enter the general circulation and be excreted into the

TABLE 2.—*Normal Observations on the Blood*

Determination	Values	Authors
Reticulated cells	0.3-1.4	Howes (Boston M. & S. J. **161**: 496, 1909)
	0.5	Davidson (Lancet **2**: 1014, 1928)
	0.2-0.8	Krumbhaar (J. Lab. & Clin. Med. **8**: 11, 1922)
Icteric index	2.5-5.0	Stetten (Am. Surg. **76**: 191, 1922)
	3.5-5.5	St. George and Brown (Arch. Int. Med. **36**: 847 [Dec.] 1925)
	3.0-5.0	Hymans (Arch. f. klin. Med. **110**: 540, 1913)

TABLE 3.—*Anemias Associated with Infection in Infancy and Childhood*

- Hemotoxic (circulating blood)
  - Blood
    - Bacterial
      - Acute infection
      - Sepsis
      - Malaria
    - Chemical
      - Lead
      - Arsenic, etc.
  - Spleen (hemolytic icterus)
- Myelotoxic (bone marrow)
  - (a) Medullary (chronic infectious diseases)
  - (b) Myelophthisic (leukemias)
  - (c) Myelopathic (pernicious anemia)

urine. Excessive urobilinuria and increase in plasma bilirubin may result from two entirely different pathologic processes—hepatic insufficiency or hemolysis. On the other hand, when there is complete obstruction to the excretion of bilirubin by the biliary tract, it will not reach the intestine, and no urobilinogen will be formed. Bilirubin accumulating in the plasma imparts to it a distinctly yellowish color, the depth of which is proportional to the rate of blood destruction. Jaundice occurs if this hyperbilirubinemia persists for some time. The presence of bilirubin in the serum is best demonstrated by the van den Bergh test, and the quantity determined by the icteric index of the serum.

Pneumonia produces a mild grade of anemia, with a more marked diminution in the hemoglobin than in the red cells. Of the 300 cases examined, 55 per cent showed less than 80 per cent hemoglobin and

TABLE 4.—*Lobar Pneumonia*

Case	Age	Hemoglobin, per Cent	Red Blood Cells	Reticulated Cells	Icteric Index	Diazo Reaction		Plasma Bilirubin
						Direct	Delayed	
J. A.	2 mo.	83	3,900,000	1.9	...	Neg.	Neg.	Neg.
M. C.	4 mo.	62	4,500,000	...	...	Neg.	Neg.	Neg.
V. M.	5 mo.	83	4,400,000	1.3	4.1	Neg.	Neg.	Neg.
D. L.	7 mo.	66	3,700,000	1.8	3.4	Neg.	Neg.	Neg.
H. G.	9 mo.	32	2,000,000	2.4	2.9	Neg.	Neg.	Neg.
I. C.	10 mo.	83	4,300,000	1.8	4.2	Neg.	Neg.	Neg.
H. C.	14 mo.	49	4,200,000	2.3	...	Neg.	Neg.	Neg.
E. Z.	16 mo.	53	3,900,000	2.1	6.2	Neg.	Pos.	0.8
S. C.	17 mo.	50	3,900,000	1.1	4.0	Neg.	Neg.	Neg.
R. I.	18 mo.	55	4,300,000	1.7	3.9	Neg.	Neg.	Neg.
M. C.	22 mo.	66	3,800,000	1.2	2.8	Neg.	Neg.	Neg.
F. B.	2 yr.	70	4,800,000	2.0	...	Neg.	Neg.	Neg.
C. F.	2 yr.	58	3,800,000	...	7.1	Neg.	Pos.	0.9
L. C.	3 yr.	79	5,100,000	1.4	3.5	Neg.	Neg.	Neg.
M. A.	3 yr.	82	4,000,000	1.7	...	Neg.	Neg.	Neg.
F. D.	4 yr.	80	3,300,000	1.9	2.7	Neg.	Neg.	Neg.
A. T.	4 yr.	79	5,000,000	1.5	...	Neg.	Neg.	Neg.
E. M.	5 yr.	68	4,500,000	...	...	Neg.	Neg.	Neg.
E. C.	6 yr.	60	3,000,000	1.6	1.9	Neg.	Neg.	Neg.
P. G.	7 yr.	85	4,800,000	...	2.1	Neg.	Neg.	Neg.
C. C.	8 yr.	70	4,100,000	1.5	...	Neg.	Neg.	Neg.
J. M.	9 yr.	81	3,600,000	1.8	...	Neg.	Neg.	Neg.

TABLE 5.—*Bronchopneumonia*

Case	Age	Hemoglobin, per Cent	Red Blood Cells	Reticulated Cells	Icteric Index	Diazo Reaction		Plasma Bilirubin
						Direct	Delayed	
J. N.	1 mo.	80	3,000,000	...	...	Neg.	Neg.	Neg.
I. V.	2 mo.	70	3,500,000	2.9	4.5	Neg.	Neg.	Neg.
L. M.	2 mo.	32	3,500,000	2.8	4.8	Neg.	Neg.	Neg
C. P.	2 mo.	43	3,200,000	1.9	1.8	Neg.	Neg.	Neg.
E. C.	5 mo.	81	4,500,000	1.9	...	Neg.	Neg.	Neg.
G. C.	5 mo.	88	4,200,000	2.8	5.0	Neg.	Neg.	Neg.
V. F.	6 mo.	84	4,600,000	1.0	3.9	Neg.	Neg.	Neg.
M. C.	7 mo.	64	3,800,000	3.0	5.6	Neg.	Neg.	Neg.
M. D.	7 mo.	68	3,600,000	2.8	2.8	Neg.	Neg.	Neg.
P. R.	7 mo.	60	4,700,000	...	...	Neg.	Neg.	Neg.
S. T.	8 mo.	75	4,200,000	3.9	7.2	Neg.	Neg.	Neg.
V. A.	8 mo.	62	4,200,000	3.7	8.1	Neg.	Neg.	Neg.
B. F.	9 mo.	65	4,200,000	2.1	2.9	Neg.	Neg.	Neg.
J. M.	9 mo.	75	4,900,000	4.0	6.2	Neg.	Neg.	Neg.
J. D.	10 mo.	81	4,200,000	3.9	5.1	Neg.	Neg.	Neg.
C. R.	11 mo.	47	3,300,000	...	...	Neg.	Neg.	Neg.
C. G.	1 yr.	49	4,200,000	1.0	2.8	Neg.	Neg.	Neg.
M. N.	1 yr.	78	4,700,000	1.8	5.1	Neg.	Neg.	Neg.
J. B.	1 yr.	59	4,700,000	2.1	4.8	Neg.	Neg.	Neg.
O. G.	1 yr.	49	4,200,000	1.0	2.8	Neg.	Neg.	Neg.
C. E.	2 yr.	62	3,200,000	1.7	3.0	Neg.	Neg.	Neg.
C. D.	2 yr.	77	4,000,000	...	5.8	Neg.	Neg.	Neg.
J. Z.	2 yr.	71	4,100,000	...	9.4	Neg.	Pos.	0.8
A. T.	2 yr.	70	4,500,000	...	7.9	Neg.	Neg.	Neg.
P. D.	2 yr.	51	4,100,000	2.1	3.0	Neg.	Neg.	Neg.
L. L.	2 yr.	62	3,100,000	2.1	3.4	Pos.	Pos.	1.0
G. K.	3 yr.	80	4,000,000	0.4	7.8	Neg.	Neg.	Neg.
M. G.	4 yr.	82	4,600,000	2.2	10.2	Neg.	Pos.	0.9
N. I.	5 yr.	81	4,500,000	...	5.7	Neg.	Neg.	Neg.
G. D.	6 yr.	79	4,500,000	0.6	4.1	Neg.	Neg.	Neg.
L. R.	6 yr.	80	4,400,000	1.8	3.1	Neg.	Neg.	Neg.
R. C.	7 yr.	70	4,100,000	2.1	4.8	Neg.	Neg.	Neg.
R. N.	9 yr.	90	4,300,000	2.3	3.7	Neg.	Neg.	Neg.
A. E.	11 yr.	75	4,600,000	...	5.0	Neg.	Neg.	Neg.

4,000,000 red cells per cubic millimeter, and 25 per cent of the children less than 60 per cent hemoglobin and 3,000,000 red cells per cubic millimeter. Infants were consistently more anemic than children, particularly as a result of lobar pneumonia in comparison with bronchopneumonia, in spite of the lesser duration of the lobar involvement. Pneumonias in children with a severe grade of anemia of nutritional origin were not included in the study, since we were primarily concerned with anemias secondary to infection. The anemias that were observed as a result of pneumonia appeared to develop as a result of the cumulative infectious process at the beginning of convalescence, and this was out of proportion to the diminished nutritional intake during the active stages of the infection.

TABLE 6.—*Otitis Media*

Case	Age	Hemoglobin, per Cent	Red Blood Cells	Reticulated Cells	Icteric Index	Diazo Reaction		Plasma Bilirubin
						Direct	Delayed	
E. V.	1 mo.	80	3,000,000	1.9	4.0	Neg.	Neg.	Neg.
A. G.	2 mo.	79	3,500,000	...	...	Neg.	Neg.	Neg.
F. P.	3 mo.	58	3,300,000	2.1	...	Neg.	Neg.	Neg.
F. K.	4 mo.	60	3,200,000	1.8	3.7	Neg.	Neg.	Neg.
J. R.	5 mo.	66	4,100,000	...	...	Neg.	Neg.	Neg.
E. G.	7 mo.	55	3,000,000	1.9	4.1	Neg.	Neg.	Neg.
H. C.	9 mo.	66	4,900,000	2.1	5.0	Neg.	Neg.	Neg.
M. M.	10 mo.	64	3,600,000	1.8	4.2	Neg.	Neg.	Neg.
F. S.	1 yr.	53	4,900,000	...	...	Neg.	Neg.	Neg.
H. G.	13 mo.	70	4,500,000	1.4	3.1	Neg.	Neg.	Neg.
E. Z.	16 mo.	53	3,900,000	1.6	3.6	Neg.	Neg.	Neg.
V. A.	20 mo.	67	4,000,000	...	...	Neg.	Neg.	Neg.
D. V.	23 mo.	68	3,900,000	...	...	Neg.	Neg.	Neg.
R. O.	2 yr.	62	4,000,000	1.4	2.9	Neg.	Neg.	Neg.
Y. M.	2¼ yr.	50	5,100,000	1.4	5.2	Neg.	Neg.	Neg.
J. T.	2¼ yr.	60	4,200,000	...	...	Neg.	Neg.	Neg.
G. I.	2¾ yr.	60	4,500,000	...	...	Neg.	Neg.	Neg.
P. E.	3 yr.	68	4,100,000	...	...	Neg.	Neg.	Neg.
R. W.	3½ yr.	70	4,200,000	1.1	3.9	Neg.	Neg.	Neg.
F. D.	4 yr.	80	3,300,000	1.6	4.7	Neg.	Neg.	Neg.
G. S.	4¾ yr.	79	2,800,000	1.1	3.9	Neg.	Neg.	Neg.
M. H.	7½ yr.	83	4,600,000	...	...	Neg.	Neg.	Neg.
F. B.	9¼ yr.	90	4,500,000	...	...	Neg.	Neg.	Neg.

The activity of blood regeneration in response to pneumonic processes was indicated by the presence of immature and nucleated erythrocytes to about the same extent in bronchopneumonia as in lobar pneumonia. The percentage of reticulocytes was found to be slightly increased, ranging to 4 per cent, in comparsion with the average normal values observed in children of about 1 per cent. Stained smears always showed the presence of normoblasts, both mature and immature. Most of the cases of pneumonia observed showed no signs of increased blood destruction, as evidenced by the level of the icteric index below 5 and by the negative plasma bilirubin below 0.5 per cent and the negative direct and delayed diazo reactions. But several severe cases of pneumonia in children with positive blood cultures showed signs of increased blood destruction, as indicated by the relatively high plasma pigments giving delayed diazo reaction. One child with bronchopneumonia in

the series showed an increased plasma bilirubin of 1, which gave a prompt direct diazo reaction owing to liver injury.

Acute otitis media as a common infection in infants produces a mild anemia as a result of depressed myeloid function. There is no evidence of blood destruction. The systemic effect of the infection was no greater on bone marrow than on alimentary dysfunction.

Congenital syphilis in infancy produces a mild but persistent hypochromic anemia. The reticulocyte content of the blood is below normal, indicating a slow erythropoietic response in the presence of the great demand on the part of the blood in the early months of life. The icteric index is not elevated nor is the plasma bilirubin content, thus indicating definite evidence against increased blood destruction in syphilis. The diazo reaction was negative in every case. From the number of cases studied, it appears that infants born with syphilitic manifestations

TABLE 7.—*Congenital Syphilis*

Case	Age	Hemoglobin, per Cent	Red Blood Cells	Reticulated Cells	Icteric Index	Diazo Reaction		Plasma Bilirubin
						Direct	Delayed	
A. D.	13 days	110	5,100,000	1.5	4.6	Neg.	Neg.	Neg.
A. G.	1 mo.	43	2,300,000	1.1	4.6	Neg.	Neg.	Neg.
C. P.	2 mo.	43	3,200,000	1.7	3.1	Neg.	Neg.	Neg.
E. A.	7 mo.	68	4,500,000	1.9	4.0	Neg.	Neg.	Neg.
R. G.	8 mo.	58	3,500,000	1.1	4.1	Neg.	Neg.	Neg.
F. S.	12 mo.	53	4,900,000	1.7	4.0	Neg.	Neg.	Neg.
J. P.	12 mo.	32	3,300,000	1.0	3.1	Neg.	Neg.	Neg.
J. S.	17 mo.	46	3,900,000	1.3	...	Neg.	Neg.	Neg.
J. L.	18 mo.	44	3,600,000	1.7	4.0	Neg.	Neg.	Neg.
M. S.	22 mo.	81	5,000,000	1.8	4.5	Neg.	Neg.	Neg.
I. S.	4 yr.	68	3,500,000	...	...	Neg.	Neg.	Neg.

show severe grades of anemia, while infants revealing syphilitic manifestations only after several weeks of life show relatively mild but persistent anemia. In fact, the less marked the clinical characteristics of syphilis, the less severe the anemia. Severe grades of anemia are associated with visceral and bone syphilis. The bone involvement has been observed by roentgenogram, and actual bone marrow infiltration by histologic section. Antisyphilitic treatment exerts no influence for some time on the severe grades of anemia associated with visceral and bone syphilis. The old contention of Flesh [3] that congenital syphilis presents a specific type of anemia has been disproved by Kleinschmidt [4] and Frank.[5] They were the first to demonstrate that anemia associated with syphilis is aplastic. Our data substantiate these findings to the extent that they show that anemia associated with syphilis is due to depression in the rate of regeneration of hemoglobin and red cells.

3. Flesh, H.: Deutsche med. Wchnschr. **27**:1090, 1907.
4. Kleinschmidt: Jahrb. f. Kinderh. **83**:87, 1916.
5. Frank: Monatschr. f. Kinderh. **31**:470, 1926.

Tuberculosis in childhood produces none of the severe grades of anemia that are observed in other chronic infectious diseases. In fact, normal hemoglobin values may often be seen in the course of active miliary tuberculosis. The data show that the anemia present is due to a diminution in the rate of regeneration in hemoglobin and red cells as a result of toxic injury from the tuberculous infection. Tuberculous involvement of the bone and peritoneum usually produces a more severe grade of anemia.

TABLE 8.—*Tuberculosis*

Case	Age	Hemoglobin, per Cent	Red Blood Cells	Reticulated Cells	Icteric Index	Diazo Reaction		Plasma Bilirubin	Comment
						Direct	Delayed		
R. S.	7 mo.	79	5,200,000	1.5	3.6	Neg.	Neg.	Neg.	Miliary
G. C.	8 mo.	87	4,200,000	1.8	4.1	Neg.	Neg.	Neg.	Peritoneal
S. T.	8 mo.	75	4,200,000	1.4	3.9	Neg.	Neg.	Neg.	Lungs
B. B.	9 mo.	77	4,500,000	1.8	...	Neg.	Neg.	Neg.	Miliary
J. J.	16 mo.	71	5,100,000	1.2	4.0	Neg.	Neg.	Neg.	Meningitis
N. C.	17 mo.	75	5,000,000	1.9	3.8	Neg.	Neg.	Neg.	Meningitis
L. A.	20 mo.	85	5,200,000	1.7	...	Neg.	Neg.	Neg.	Miliary
E. M.	2 yr.	53	4,600,000	...	4.2	Neg.	Neg.	Neg.	Miliary
P. G.	2 yr.	60	4,600,000	...	...	Neg.	Neg.	Neg.	Miliary
G. K.	3 yr.	50	5,700,000	1.0	4.6	Neg.	Neg.	Neg.	Miliary
S. T.	4 yr.	87	4,700,000	1.9	3.8	Neg.	Neg.	Neg.	Miliary
D. C.	4 yr.	75	4,600,000	2.1	4.6	Neg.	Neg.	Neg.	Miliary
J. O.	5 yr.	62	3,900,000	2.5	4.2	Neg.	Neg.	Neg.	Miliary

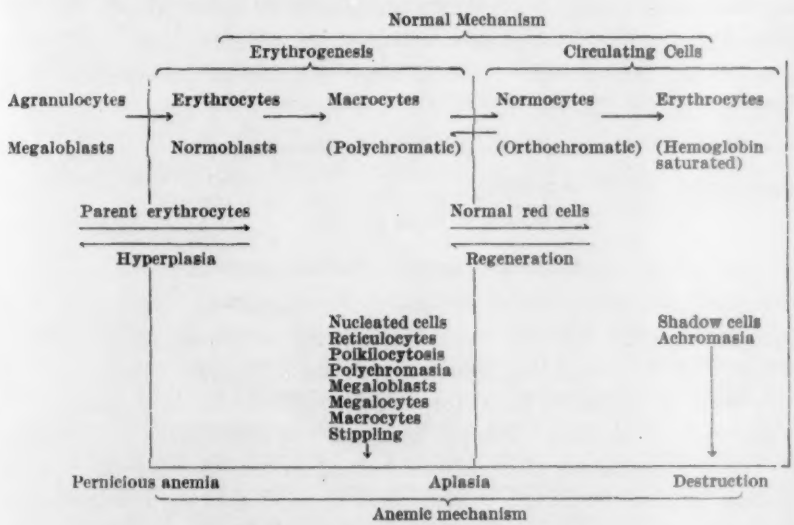
TABLE 9.—*Chronic Infections*

Case	Age	Hemoglobin, per Cent	Red Blood Cells	Reticulated Cells	Icteric Index	Diazo Reaction		Plasma Bilirubin	Disease
						Direct	Delayed		
J. D.	4 mo.	51	2,800,000	1.2	3.4	Neg.	Neg.	Neg.	Nephritis
W. B.	1 yr.	47	4,700,000	1.7	2.9	Neg.	Neg.	Neg.	Nephritis
R. B.	10 yr.	68	4,000,000	1.9	3.2	Neg.	Neg.	Neg.	Nephritis
L. S.	10 yr.	85	4,200,000	2.5	3.7	Neg.	Neg.	Neg.	Nephritis
M. L.	12 yr.	60	3,800,000	2.1	3.9	Neg.	Neg.	Neg.	Nephritis
A. L.	1 yr.	70	3,900,000	1.4	2.9	Neg.	Neg.	Neg.	Dysentery
G. B.	2 yr.	69	3,800,000	1.5	3.4	Neg.	Neg.	Neg.	Dysentery
R. C.	7 yr.	80	4,000,000	...	...	Neg.	Neg.	Neg.	Dysentery
E. R.	10 yr.	70	4,000,000	1.2	2.7	Neg.	Neg.	Neg.	Osteomyelitis
V. B.	4 mo.	80	4,000,000	1.8	3.6	Neg.	Neg.	Neg.	Vincent's disease
D. A.	4 mo.	79	4,100,000	2.4	2.9	Neg.	Neg.	Neg.	Vincent's disease

Anemia associated with chronic nephritis does not become evident until several weeks have elapsed after renal injury. The reticulated cell content is low, indicating sluggish red cell regeneration by the bone marrow. The direct diazo reaction is negative, and so is the plasma bilirubin. The anemia, therefore, is due to diminished erythrogenic function wherein the rate of replacement of red cells falls short of the usual normal rate of blood destruction. There is no evidence that hydremia is responsible for the anemia of chronic nephritis. Rarely are hemolytic substances present in the blood serum in chronic nephritis. The erythrocytes of stained smears of the blood are reduced in size, but

poikilocytosis is rare, and achromia is mild. The severity and chronicity of the anemia appear proportional to the toxic injury responsible for the renal involvement.

Sepsis shows a rapidly developing anemia of low color index. The reticulocyte count is usually diminished, the plasma pigment gradually increased to the extent that bilirubin gives a prompt diazo reaction. This probably indicates liver damage due to focal lesions set up by the septic process. Under such conditions the direct diazo reaction fails as an index of blood destruction, because bilirubin of hepatic origin will give the prompt diazo reaction even if there be at the same time an increase in bilirubin due to blood destruction. Hemolytic substances, however, are present in the blood in septicemia due to Streptococcus hemolyticus, but are not present in bacteremia due to Streptococcus viridans in subacute bacterial endocarditis. In the former, toxic substances elaborated produced blood destruction, while in the latter they merely depressed bone marrow function and produced some liver damage that is responsible for the increase of plasma bilirubin.



COMMENT

Studies of the mechanism of anemia approached from the status of the peripheral circulation give only a first approximation of the nature of the process. It is in the functional physiochemical changes in the bone marrow occurring in the course of anemia that an insight into its fundamental mechanism can eventually be gleaned. The myelogenous changes constitute the first cause, while the hematogenous changes are end-results in anemia. Therefore, intrinsic elucidation of the problems of hematology rests on cellular, rather than on humeral, pathology. For

blood is not a living tissue, but a passive vehicle for the living tissues of the body. Even the blood corpuscles function in as passive a manner as do all its other components. Deviations from the normal in blood hemoglobin and erythrocytes must therefore be regarded as symptomatic of disturbance in the hematopoietic tissues. The changes in the blood are due either to direct action on the circulating corpuscles or, more often, to a stimulation or depression of the hematopoietic tissues. Blood studies alone reveal the functional capacity and reacting power of the bone marrow, which are of greater diagnostic than of mechanistic significance.

Anemia is not only a reduction in the normal amount of hemoglobin and erythrocytes of the blood, but a diminution in the other components of blood, in the white cells, in the platelets and in the blood volume. These changes indicate the state of the blood that is symptomatic of a great variety of diseases. Anemia associated with infection is the result of injury to the erythropoietic tissue of the marrow rather than to the cells that are present in the circulating blood. It is a manifestation of marrow insufficiency. It consists of a disturbance in the relation between blood demand for red cells and bone marrow supply. It is therefore a myelopathy. The dynamic equilibrium existing between blood and bone marrow may be expressed thus:

$$\text{Myeloid function} \rightleftarrows \text{Blood requirement}$$

Applying the law of mass action,

$$\frac{\text{Concentration of blood required}}{\text{Concentration of myeloid produced}} = \text{Constant}$$

Anemia results if the numerator is increased in accelerated metabolism during fever, and the denominator is not proportionately increased to maintain the normal equilibrium constant. Myeloid insufficiency in the course of increased blood-forming demand results in anemia, acute or chronic. It is uncompensated bone marrow function.

The intermediated mechanism involved in the stimulation of bone marrow function by an accelerated blood demand is as yet unknown. In the respiratory mechanism there is an intermediate nerve center; in the carbohydrate metabolism there is an intermediate pancreatic control; in the acid-base metabolism there is an intermediate buffer regulation. But in the hematopoietic mechanism it must be assumed for the present that actual blood deficiency stimulates erythropoietic activity without any specific intermediate mechanism. The levels of blood deficiency and of bone marrow activity may be evaluated approximately, according to Douglas and Tannenbaum,[6] in terms of the blood content in certain

6. Douglas, A. H., and Tannenbaum, H.: Mechanism of Secondary Anemia, Arch. Int. Med. **45**:252 (Feb.) 1930.

red cell products as presented in the foregoing data. Thus is a more definite notion obtained of the nature of hematopoietic injury in the course of infection.

Infectious injury to the blood-forming organs has been observed experimentally from several standpoints. Dragstedt [7] showed that normally the intestinal mucous membrane prevents the absorption of toxic substances, but that in avitaminosis and in infection this protective mechanism is impaired. Koessler and Hanke [8] further observed that the intestinal epithelium can render certain toxins inert, but not in the course of infection. Cannon [9] found no significant changes in the blood picture when chronic stasis with proteolytic intestinal flora was present for weeks. But once intercurrent infection supervened, the body lost the protective mechanisms preventive of bone marrow injury.

Toxic injury to the bone marrow produced by infection has been demonstrated experimentally in animals by Fejes.[10] Histologic sections of bone marrow altered by infection have been shown by Naegeli to be a compensatory hypoplasia of bone marrow cells at the expense of fat cells. Hypochromia in these anemias associated with infection may be interpreted on the basis that hemoglobin saturation of young cells is the last stage of erythropoiesis. And in hasty regeneration polychromatophilia is a necessary consequence. Whipple recently demonstrated that the stroma of the red cell is synthesized by the liver from its available store of amino-acids. Therefore it is only in liver injury, occurring, for example, in the course of sepsis, that the erythrocyte content of the blood is markedly diminished.

Infection depresses the rate of regeneration of hemoglobin and erythrocytes. The retardation in myeloid function parallels the severity of the infection, being rapid in acute streptococcus infection and slow but cumulative in chronic pyogenic infections. The data for chronic infections—syphilis, tuberculosis and nephritis—show conclusively that the rate of regeneration of red cells is not accelerated to meet their rapid utilization resulting from an increased metabolism. Infectious injury to the bone marrow diminishes the erythropoietic response. The red cells are small, with diminished adsorption for stain. Immature forms indicative of active regeneration are in the minutia. Such anemia is a hypochromic anemia of low color index, with evidences of parent cell destruction giving rise to poikilocytosis and oligochromasia, as has also been recorded by Halbertsma.[11] In acute infections, as pneumonia and

7. Dragstedt: J. Exper. Med. **30**:109, 1919.
8. Koessler and Hanke: J. Biol. Chem. **44**:889, 1924.
9. Cannon: J. Infect. Dis. **43**:488, 1928.
10. Fejes: Deutsches Arch. f. klin. Med. **102**:129, 1911.
11. Halbertsma, T.: The Amount of Blood to be Transfused in Anemia of Children, Am. J. Dis. Child. **24**:269 (Oct.) 1922.

otitis media, the regeneration of red cells is depressed, though there is more evident response, as judged by macrocytes and macroblasts in the blood. The color index is higher, and there is a distinct reversion to the late embryonic type of erythropoiesis.

Infection may produce anemia by actual destruction of the circulating blood. This is the essential mechanism in the hemolytic anemias. Hemolytic substances isolated from streptococci, the malarial and intestinal parasites, have a specific toxic effect on the red cells in the form of increased hemolysis. Though normally blood destruction is continuous by fragmentation and phagocytosis, bone marrow produces just a sufficient number of red cells to replace those destroyed. The two phenomena presented by mitochondria and reticulum, parallel the amount regenerated from day to day. In infections wherein the disturbance is primarily in the circulating blood, the bone marrow suffers merely from an excessive demand which is out of all proportion to its capability of immediate response. In fact, in persistent toxic injury and destruction of red cells the bone marrow escapes somewhat. The normal continuous erythroplastic activity is not sufficient to cope with the loss, and so a temporary erythrogenerative mechanism reenforces the physiologic one. The blood picture shows little change in the type of cells, except that the hasty regeneration is evidenced by immature forms, reticulated cells, normoblasts and polychromatophilia.

CONCLUSIONS

1. Anemia associated with infection results from either diminished production of erythrocytes or increased destruction of circulating erythrocytes.

2. The younger the infant the more widespread the erythrogenic islets, and, therefore, the more susceptible the labile hemogenic-hemolytic equilibrium.

3. The normal reticulocyte content is higher in infants than in adults because of relatively greater blood demand, and the normal icteric index is correspondingly elevated because of the relatively greater physiologic red cell destruction.

4. Infection depresses the rate of regeneration of hemoglobin and red cells, rapid in acute streptococcus invasions and slow but cumulative in chronic infections. The hypochromia is due to the excessive blood demand, which makes the last stage, hemoglobin saturation, incomplete. Marked diminution in red cells is due to associated liver damage, thereby interfering with erythrocyte synthesis from the store of available amino-acids. Sepsis increases the rate of blood destruction and produces liver damage by focal lesions.

5. Anemia associated with infection is a manifestation of bone marrow insufficiency, because of the shift in the normal equilibrium between blood demand and bone marrow supply:

$$\frac{\text{Concentration of erythrocytes required}}{\text{Concentration of myeloid produced}} = \text{Constant}$$

Anemia results if the numerator is increased in accelerated metabolism during fever and the denominator is prevented by infection from increasing in order to keep the normal equilibrium constant.

PHOSPHORUS METABOLISM IN INFANTS

A COMPARATIVE STUDY OF THE PHOSPHORUS METABOLISM OF HEALTHY INFANTS FED BREAST MILK AND COW'S MILK *

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Although the mineral metabolism of healthy infants has been studied rather intensively by numerous investigators, in few instances has the same child been used as the basis for a comparative study of breast milk and cow's milk. As stated in a previous report, the chief purpose of this investigation was to exclude the possibility of obtaining results that might be interpreted as being due to constitutional differences in the experimental subjects. Therefore this study was conducted on a group of five normal, healthy infants, each of whom during alternate periods (three days each) was given breast milk and cow's milk mixtures.

REVIEW OF LITERATURE

A survey of the literature shows that many phases of the phosphorus metabolism of infants have been investigated, but there is a striking paucity of information concerning the comparative phosphorus metabolism of healthy infants as studied in the same subject. The results of previous investigators have been arranged in two groups for convenience in comparison. Table 1 represents the data obtained by various investigators who studied the phosphorus metabolism in healthy infants fed on breast milk. Table 2 is a similar résumé for infants fed on modified cow's milk mixtures.

The work done by Keller [1] in 1900 furnishes the only data obtainable in which the same infant was used for comparison. He found that considerably more phosphorus was eliminated by the artificially fed infants than by the breast-fed ones, regardless of the strength of the cow's milk mixtures (tables 1 and 2). Although the absolute quantity of retained phosphorus was greater in those artificially fed, the phosphorus of breast milk was utilized relatively better than that of

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* From the Nelson Morris Memorial Institute for Medical Research and the Sarah Morris Hospital for Children, Pediatric Division of the Michael Reese Hospital.

1. Keller, A.: Phosphor und Stickstoff im Säuglings-Organismus, Arch. f. Kinderh. **29**:1, 1900.

TABLE 1.—*Phosphorus Metabolism per Twenty-Four Hours of Healthy Infants Fed Breast Milk*

Author	Age, Mo.	Body Weight, Kg.	Phosphorus Pentoxide Intake		Phosphorus Pentoxide Output			Phosphorus Pentoxide Absorption			Phosphorus Pentoxide Retention		
			Gm.	Gm. per Kg. of Weight	Urine, Gm.	Feces, Gm.	Total, Gm.	Gm.	Gm. per Kg.	Intake, per Cent	Gm.	Gm. per Kg.	Intake, per Cent
Birk: Monatschr. f. Kinderh. **9**: 595, 1910 (colostrum)	Newborn	3.87	0.234	0.060	0.044	0.003	0.048	0.230	0.059	98.0	0.185	0.047	79.0
	Newborn	2.97	0.054	0.018	0.060	0.025	0.085	0.028	0.009	52.8	—0.032	.....	....
Michel: Obstérique **1**: 518, 1897 (baby I).....	Newborn	....	0.323	.....	0.020	0.020	0.040	0.303	.....	92.7	0.282	.....	87.3
(baby II).....	Newborn	....	0.220	.....	0.025	0.025	0.050	0.195	.....	88.6	0.170	.....	77.3
(baby III)....	Newborn	....	0.263	.....	0.018	0.034	0.052	0.245	.....	93.2	0.211	.....	80.2
Peiser: Jahrb. f. Kinderh. **81**: 437, 1915													
Baby Band	1.5	3.88	0.289	0.074	0.103	0.064	0.167	0.225	0.058	77.8	0.123	0.031	42.5
Baby Leb	1.5	3.85	0.228	0.059	0.090	0.079	0.169	0.149	0.038	65.3	0.058	0.015	25.5
Keller: Arch. f. Kinderh. **29**: 1, 1909													
Exper. no. 3.....	2.0	4.35	0.324	0.074	0.098	0.051	0.149	0.273	0.062	84.4	0.175	0.040	54.1
Exper. no. 4.....	2.25	4.38	0.240	0.054	0.061	0.050	0.111	0.190	0.043	79.2	0.128	0.029	53.5
Tobler: Monatschr. f. Kinderh. **9**: 210, 1910 (exper. no. 11).....	2.5	4.08	0.210	0.051	0.057	0.034	0.091	0.175	0.043	83.7	0.118	0.029	56.5
Lindberg: Ztschr. f. Kinderh. **16**: 90, 1907													
Exper. no. 1.....	2.5	4.28	0.294	0.068	0.046	0.055	0.101	0.238	0.055	81.2	0.192	0.044	65.4
Exper. no. 2.....	2.75	4.37	0.288	0.066	0.087	0.061	0.149	0.227	0.051	78.6	0.139	0.031	48.3
Klotz: Jahrb. f. Kinderh. **70**: 15, 1909.....	2.5	3.42	0.089	0.026	0.035	0.027	0.062	0.062	0.018	69.7	0.027	0.008	30.3
Muhl: Acta pædiat. **2**: 1, 1924 (baby B.I)...	2.5	5.49	0.251	0.045	0.071	0.059	0.130	0.191	0.034	76.0	0.120	0.022	48.0
(baby B.II)..	2.5	5.56	0.261	0.046	0.094	0.054	0.148	0.207	0.037	79.0	0.113	0.020	43.0
Michel and Perrett: Bull. Soc. d'obst. de Par. **1**: 98, 1899	3.0	4.72	0.268	0.056	0.075	0.071	0.146	0.196	0.040	73.2	0.121	0.025	45.2
Malmberg: Acta pædiat. **2**: 209, 1923													
Baby S. E.	3.5	5.44	0.359	0.066	0.077	0.071	0.148	0.288	0.052	80.0	0.211	0.038	59.0
Baby O. G.	3.5	5.44	0.332	0.061	0.036	0.062	0.099	0.270	0.049	81.0	0.234	0.043	70.0
Muhl (baby L. St. I).....	4.0	5.14	0.289	0.056	0.117	0.046	0.163	0.243	0.047	84.0	0.126	0.024	44.0
Blauberg: Ztschr. f. Biol. **40**: 36, 1900.....	5.0	6.74	0.203	0.030	0.088	0.022	0.110	0.181	0.026	89.2	0.093	0.013	45.9

TABLE 2.—*Phosphorus Metabolism per Twenty-Four Hours of Healthy Infants Fed Cow's Milk (Modified)*

Author	Age, Mo.	Body Weight, Kg.	Phosphorus Pentoxide Intake		Phosphorus Pentoxide Output			Phosphorus Pentoxide Absorption			Phosphorus Pentoxide Retention		
			Gm.	Gm. per Kg. of Weight	Urine, Gm.	Feces, Gm.	Total, Gm.	Gm.	Gm. per Kg. of Weight	Intake, per Cent	Gm.	Gm. per Kg. of Weight	Intake, per Cent
Peiser: Jahrb. f. Kinderh. **81**: 437, 1915													
Baby Leb.	2	Eiweiss milk	0.980	.....	0.463	0.445	0.908	0.535	.....	54.5	0.730	.....	7.4
Baby Gl.	2.25	Eiweiss milk	1.022	.....	0.506	0.412	0.918	0.610	.....	59.6	0.085	.....	8.5
Baby Cz.	4	Eiweiss milk	1.203	.....	0.510	0.500	1.010	0.703	.....	58.4	0.193	.....	15.8
Keller: Arch. f. Kinder. **29**: 1, 1900 (exper. 12)	2.75	4.90	0.824	0.168	0.410	0.1073	0.517	0.717	0.146	87.1	0.306	0.062	37.2
Cronheim and Müller: Biochem. Ztschr. **9**: 76, 1908 (baby 1)	4	3.84	1.359	0.353	0.626	0.375	1.001	0.984	0.256	72.4	0.358	0.092	26.3
(baby 2)	6	8.14	2.208	0.271	0.981	0.740	1.721	1.468	0.180	66.4	0.487	0.059	22.6
Bruck (baby U)	3	3.4	0.719	0.211	0.427	0.1251	0.5522	0.594	0.174	82.6	0.1675	0.049	23.5
(baby Sch.)	8.5	5.6	1.454	0.259	0.836	0.3173	1.1536	1.136	0.202	79.4	0.3005	0.053	26.3
Blauberg: Ztschr. f. Biol. **40**: 1, 1900	?	7.5	2.060	0.274	0.589	0.9627	1.5526	1.098	0.146	53.2	0.5079	0.067	24.2
Hoobler: Am. J. Dis. Child. **2**: 107 (Aug.) 1912													
4.0% fat	9	7.8	2.741	0.351	2.009	0.5991	2.6081	2.142	0.274	78.1	0.1336	0.017	4.8
5.4% fat	9.5	7.9	2.234	0.282	1.336	0.3789	1.7149	1.855	0.235	83.0	0.5196	0.065	27.7
2.1% fat	10	8.3	2.215	0.266	1.152	0.7648	1.9168	1.450	0.174	67.0	0.3320	0.040	14.5
Telfer: Quart. J. Med. **51**: 45, 1912													
Baby 1	8	6.5	2.20	0.338	0.930	0.940	1.870	1.260	0.193	57.2	0.330	0.050	15.0
Baby 2	15	8.3	2.20	0.265	1.170	1.050	2.22	1.150	0.138	52.2	—0.020	.....	....

cow's milk. Keller concluded that the absorption of phosphorus is not dependent on the quantity of phosphorus intake. He also noted that the absorption and retention of phosphorus are relatively better in the younger infants, being best in the new-born. However, in Keller's study, daily determinations of the phosphorus in breast milk were not made, but a mixture of daily samples was analyzed, and the figure was used as an average for the entire investigation.

In 1877, Cruse studied a large number of normal breast-fed infants, whose ages varied from 2 to 60 days. He examined the urine only and found that during the first few days of life there is an absence of phosphate or only traces, and that with increasing age a definite phosphorus content is established.

Michel [2] investigated the nitrogen and inorganic salt metabolism in normal breast-fed infants from 5 to 15 days old (table 1). He concluded that in normal breast-fed new-born infants the ingested phosphorus was almost completely utilized. His figures showed an average of 92.5 per cent absorption and 89.6 per cent retention. It has been claimed by Keller and others that these values were probably too high, because the phosphorus derived from the intestinal secretions and destruction of intestinal epithelium were reckoned as unabsorbed phosphorus intake.

Cronheim and Müller,[3] in 1908, experimented with boiled, raw and pasteurized milk mixtures on two normal infants and two rachitic infants. They found that the highest values for phosphorus absorption and retention were obtained with the boiled milk (table 2). They also noted that phosphorus absorption is greatly increased when egg yolk is added to the feeding.

Moll's [4] investigations of normal breast-fed infants were limited to the phosphate analyses of urine without consideration of the intake and the output. These studies showed no phosphate in infants with nutritional disturbances, even of the mildest forms.

In his studies on phosphorus and calcium metabolism of breast-fed premature infants, Hamilton [5] pointed out that there is a striking parallelism between the phosphorus intake and the excretion of phosphorus in the feces in both normal and premature infants. In rapidly growing premature infants with a low phosphorus intake the amount

2. Michel, R.: Sur le lait de femme et l'utilisation de ses matériaux nutritifs, Obstétrique **1**:518, 1897.

3. Cronheim, W., and Müller, E.: Stoffwechselversuche an gesunden und rachitischen Kindern mit besonderer Berücksichtigung des Mineralstoffwechsels, Biochem. Ztschr. **9**:76, 1908.

4. Moll, L.: Die klinische Bedeutung der Phosphorausscheidung im Harn beim Brustkind, Jahrb. f. Kinderh. **29**:129, 1909.

5. Hamilton, B.: The Calcium and Phosphorus Metabolism of Prematurely Born Infants, Acta pædiat. **2**:1, 1922.

of phosphorus excreted in the urine may be almost negligible. According to Hamilton, the phosphorus retention is almost as great in most premature infants as in the normal infant. He observed that the excretion of phosphorus does not follow the constant level maintained by calcium excretion. With a low phosphorus intake, a considerable amount is retained and the excretion is very low. The retention is evidently more important than the excretion. When the phosphorus intake increases, the excretion also increases.

Hoobler [6] determined the phosphorus exchange in a 9 months old infant fed on cow's milk with (1) low, (2) medium and (3) high fat content. His results showed 76.0 per cent, 78.1 per cent and 83 per cent absorption, respectively (table 2). These figures indicate that phosphorus is more readily absorbed in the presence of an increased quantity of fat when the infant receives cow's milk.

In his observations on two infants, one 8 months and the other 15 months of age, Telfer [7] found that the total amount of calcium and phosphorus eliminated was nearly proportional to the intake. No evidence was obtained that mineral matter from endogenous sources was excreted in the feces to any appreciable extent. According to Telfer, 40 per cent of the total phosphorus excreted appeared in the urine and 60 per cent in the feces (table 2). With acid formation in the intestine, less phosphorus was excreted by the feces and more by the urine.

Lindberg [8] conducted an intensive metabolic study of the fat, nitrogen, potassium, sodium, calcium, magnesium and phosphorus in a 2½ months old breast-fed infant, with special reference to the effect of increased fat intake on the metabolic exchange of the various minerals mentioned. He obtained higher values for phosphorus retention in the breast-fed infant than had any previous investigator (table 1). With an increased fat intake the phosphorus absorption and retention were considerably impaired; he explained this fact by the increased elimination through the urine.

DESCRIPTION OF EXPERIMENT

Details of the management of this investigation and the preparation of the excretions have been described in a previous article.[9] The phosphorus was deter-

6. Hoobler, B. R.: The Rôle of Mineral Salts in the Metabolism of Infants, Am. J. Dis. Child. **2**:107 (Aug.) 1912.

7. Telfer, S. V.: Studies on Calcium and Phosphorus Metabolism: The Excretion of Calcium and Phosphorus, Quart. J. Med. **51**:45, 1912.

8. Lindberg, G.: Ueber den Stoffwechsel des gesunden, natürlich ernährten Säuglings und dessen Beeinflussung durch Frauenmilchfett, Ztschr. f. Kinderh. **16**:90, 1917.

9. Wang, C. C.; Witt, D. B., and Felcher, A. R.: A Comparison of the Metabolism of Some Mineral Constituents of Cow's Milk and of Breast Milk in the Same Infant, Am. J. Dis. Child. **27**:352 (April) 1924.

mined as total phosphorus, no attempt being made to differentiate inorganic and organic phosphate.

The modified ceruleomolybdate method described by Deniges[10] was employed for the determination of the phosphorus in the milk, as well as in the excretions. The analyses of milk and urine were made with specimens of 1 cc. each. For the analyses of the feces, dried specimens were used the weights of which varied from 0.1188 Gm. to 0.4843 Gm. The final estimations for each sample were made with a colorimeter instead of a series of specially prepared standards as described by Deniges. The results give the quantity of total phosphorus expressed as phosphorus pentoxide. All determinations were made in duplicate.

COMMENT

The analyses of individual twenty-four hour specimens have little or no value for metabolic investigations. Considerable variation in the amounts of phosphorus eliminated daily were noted in many instances. For convenience in comparison with the work of others, the averages of three consecutive twenty-four hour periods are used (table 3). These results show distinct differences produced by change of diet.

Differences in the Quantity of Phosphorus Excretion Produced by Change of Milk.—In the infants studied in this investigation the phosphorus intake is invariably much greater on feedings of modified cow's milk than of breast milk; with cow's milk it varied from 0.403 to 0.935 Gm. per twenty-four hours, with an average of 0.654 Gm. The corresponding figures for breast milk are from 0.187 to 0.312 Gm., with an average of 0.258 Gm. The phosphorus intake reported by other investigators studying breast-fed infants varied from 0.054 Gm. to 0.359 Gm. per twenty-four hours, with an average of 0.251 Gm. (table 1). The intake per kilogram of weight during the periods when the infant was fed on breast milk varied from 0.04 to 0.078 Gm., with an average of 0.056 Gm.; on cow's milk, the intake per kilogram ranged from 0.118 to 0.146 Gm., with an average of 0.135 Gm. The intake per kilogram as determined by other investigators ranged from 0.018 to 0.081 Gm. per twenty-four hours, with an average of 0.055 Gm. Most of the infants used by other investigators for the study of cow's milk (as shown in table 2) were considerably older than those studied in this investigation. Therefore only the more significant data will be used for comparison.

In this investigation the phosphorus output through the urine varied from 0.043 to 0.088 Gm. per twenty-four hours (table 3) during the periods when the infant was fed breast milk, whereas the corresponding

10. Deniges, G.: Determination quantitative des plus faibles quantités de phosphates dans les produits biologiques par la méthode céruleomolybdique, Compt. rend. Soc. de biol. **84**:875, 1921.

TABLE 3.—*Average Daily Phosphorus Metabolism of Normal Infants*

Name	Age, Mo.	Body Weight, Kg.	Kind of Milk	Phosphorus Pentoxide Intake		Phosphorus Pentoxide Output				Phosphorus Pentoxide Absorption			Phosphorus Pentoxide Retention		
				Gm.	Gm. per Kg. of Weight	Urine, Gm.	Feces, Gm.	Total, Gm.	Total Gm. per Kg. of Weight	Gm.	Gm. per Kg. of Weight	Intake, per Cent	Gm.	Gm. per Kg. of Weight	Intake, per Cent
W. O.	2.6	4.13	Breast	0.240	0.058	0.064	0.041	0.105	0.025	0.199	0.048	83.0	0.135	0.032	56.0
W. O.	3.0	4.39	Cow's	0.632	0.144	0.265	0.086	0.351	0.080	0.546	0.124	86.2	0.281	0.064	44.2
W. O.	3.3	4.46	Breast	0.308	0.069	0.084	0.059	0.143	0.031	0.249	0.055	80.6	0.165	0.037	53.5
T. O.	3.2	3.57	Breast	0.187	0.052	0.045	0.016	0.061	0.017	0.171	0.047	91.2	0.126	0.035	67.1
T. O.	4.3	4.03	Cow's	0.562	0.139	0.260	0.138	0.398	0.098	0.424	0.105	75.4	0.164	0.040	29.2
E. M.	5.5	7.43	Cow's	0.935	0.126	0.357	0.178	0.535	0.072	0.757	0.101	80.9	0.400	0.053	42.8
E. M.	5.7	7.33	Breast	0.299	0.040	0.088	0.058	0.146	0.019	0.241	0.032	80.6	0.153	0.020	51.0
B. N.	0.4	3.26	Cow's	0.404	0.123	0.139	0.102	0.241	0.074	0.302	0.092	74.5	0.162	0.049	40.1
B. N.	1.4	3.61	Breast	0.274	0.075	0.043	0.059	0.102	0.028	0.215	0.059	78.2	0.172	0.047	62.5
B. B.	1.3	3.82	Cow's	0.579	0.152	0.245	0.092	0.337	0.088	0.487	0.127	84.1	0.242	0.063	41.7
B. B.	1.6	3.99	Breast	0.312	0.078	0.073	0.039	0.112	0.028	0.273	0.068	87.2	0.200	0.049	63.8
B. B.	2.1	4.54	Cow's	0.663	0.146	0.298	0.123	0.421	0.092	0.540	0.119	81.4	0.242	0.053	36.5
B. B.	2.4	4.74	Breast	0.215	0.045	0.055	0.038	0.093	0.019	0.177	0.037	82.1	0.122	0.026	56.6
B. B.	4.6	5.56	Breast	0.227	0.041	0.061	0.040	0.102	0.018	0.187	0.033	82.0	0.125	0.022	55.0
B. B.	6.1	6.78	Cow's	0.803	0.118	0.300	0.113	0.473	0.069	0.690	0.101	85.8	0.330	0.048	41.0

figures for the periods when cow's milk was used varied from 0.139 to 0.360 Gm. per twenty-four hours. It will also be noted that the amount of phosphorus eliminated through the urine in each period is considerably greater than the amount excreted in the feces during the same period.

From 0.016 to 0.059 Gm. of phosphorus was excreted through feces in this study, the average being 0.044 Gm. per twenty-four hours for breast milk. With cow's milk, the elimination of phosphorus in the feces varied from 0.086 to 0.178 Gm., with an average of 0.119 Gm.

The increase in the phosphorus excretion during the periods when cow's milk was used is noted more strikingly when the figures for the total phosphorus output are compared. During the periods when breast milk was given the total phosphorus output varied from 0.061 to 0.146

TABLE 4.—*Relation of Age to Phosphorus Metabolism per Twenty-Four Hours in Infants Fed Breast Milk*

Name of Subject	Age, Mo.	Phosphorus Pentoxide	
		Utilization, Gm. per Kg.	Retention, Gm. per Kg.
B. N.	1.4	0.059	0.047
B. B.	1.6	0.068	0.049
B. B.	2.4	0.037	0.026
W. O.	2.6	0.048	0.032
T. O.	3.2	0.047	0.035
W. O.	3.3	0.055	0.037
B. B.	4.6	0.033	0.022
E. M.	5.7	0.032	0.020

Gm. per twenty-four hours, while the corresponding figures for the periods when cow's milk was given ranged from 0.241 to 0.535 Gm. A comparison of the average figures shows that the total phosphate output during the periods when cow's milk was given was almost four times as great as that during the periods when breast milk was used, namely, 0.394 Gm. per twenty-four hours when cow's milk was given and 0.108 Gm. when breast milk was used.

THE EFFECT OF CHANGE OF MILK ON THE ABSORPTION AND RETENTION OF PHOSPHORUS

In this investigation the actual quantities of phosphorus absorbed by the infants studied were considerably larger during the periods when cow's milk was given. During the periods when breast milk was fed the phosphorus absorption varied from 0.171 to 0.272 Gm., with an average of 0.213 Gm. per twenty-four hours. The corresponding figures for cow's milk range from 0.301 to 0.757 Gm., with an average of 0.535 Gm. per twenty-four hours. The average percentage absorption for breast milk is 83.1 as compared to 81.1 for cow's milk.

In calculating the average figures for absorption and retention as reported by other investigators using breast milk, the data obtained by Birk [11] were not included, because neither of his two subjects are suitable for comparison with our subjects. One new-born infant showed a negative balance (see table 1). This is the only breast-fed infant in whom a negative balance has ever been reported. The phosphorus intake for this infant was very low, 0.054 Gm. per twenty-four hours, as compared to the average intake of 0.251 Gm. per twenty-four hours, as reported by all other investigators. Birk's other subject was also a new-born infant who received feedings of colostrum. The metabolic study of this child showed that only 2 per cent of the total phosphorus intake was excreted in the feces, resulting in a 98 per cent absorption. The retention was correspondingly high, 79 per cent. The aforementioned results of Michel in his study of healthy breast-fed new-born infants are in accord with these high values for absorption and retention.

The values for phosphorus absorption, as reported by other workers (table 2), are, in general, lower than those given in this report. The average absorption for breast milk is 0.196 Gm. per twenty-four hours, which is equivalent to an average absorption of 78.8 per cent. Those who experimented with cow's milk gave results that showed an average absorption of 67.9 per cent.

On analyzing the values obtained in this study for phosphorus retention (table 3), it will be noted that the actual amounts of phosphorus retained were considerably greater during the periods of cow's milk feedings. The average value for retention of phosphorus when breast milk was given was 0.149 Gm., as compared to an average of 0.260 Gm. obtained with cow's milk. The values for breast milk per kilogram varied from 0.020 to 0.049 Gm., with an average of 0.033 Gm. per twenty-four hours. With cow's milk the minimum value per kilogram was 0.04 Gm., and the maximum was 0.064 Gm. per twenty-four hours, the average being 0.053 Gm. At first glance the percentage values for phosphorus retention might indicate that there is a demarcation between the two types of feedings. In analyzing these values, one should not overlook the fact that the phosphorus intake was much greater during the periods when cow's milk was fed. Over 50 per cent of the phosphorus intake was retained by each infant during the periods when it was breast fed, the values ranging from 51 to 63.8

11. Birk, W.: Beiträge zur Physiologie des neugeborenen Kindes: III. Die Bedeutung des Kolostrums Analysen und Stoffwechsel Versuche, Monatschr. f. Kinderh. **9**:595, 1910; IV. Der Stoffwechsel des Kindes während der ersten Lebenstage bei künstlicher Ernährung, ibid. **10**:1, 1911.

per cent, with an average of 58.1 per cent. During the periods of cow's milk feedings, the retention was always below 50 per cent, the maximum being 44.2 per cent and the minimum, 29.2 per cent.

The results obtained by other investigators show less uniformity. The percentage of retention with cow's milk varied from 4.8 per cent as noted by Hoobler to 37.2 obtained by Keller (table 2). The average percentage of retention obtained with breast milk by other investigators was 45.7 per cent. Excluding the results of Birk and Michel for new-born infants, the lowest value for phosphorus retention when the diet consisted of breast milk was recorded by Peiser [12] (25.5 per cent), while the maximum was 70.0 per cent, as noted by Malmberg [13] (table 1).

THE RELATIONSHIP OF AGE TO PHOSPHORUS METABOLISM

The values for phosphorus absorption and retention per kilogram obtained with breast milk (table 4) show a diminution with increasing age. The youngest infant (B. N.) at 1.4 months showed a per kilogram absorption of 0.059 Gm. of phosphorus, whereas the oldest infant (E. M.) at 5.7 months absorbed only 0.032 Gm. per kilogram per twenty-four hours. The corresponding figures for retention showed a reduction from 0.047 to 0.020 Gm. of phosphorus. In other words, the optimal absorption and retention of phosphorus occur in the earliest months of life.

B. B. at 2.4 months was an exception, as he showed absorption and retention values almost as low as those of E. M. at 5.7 months. No explanation can be offered for this variation.

The absorption and retention of phosphorus during the periods of cow's milk feedings are apparently not influenced by age, as determined by this investigation. A table is omitted for this reason.

SUMMARY

1. The phosphorus metabolism of infants was studied in a group of five apparently normal, healthy infants, each of whom was fed breast milk and cow's milk mixtures during alternate periods. The data thus obtained would preclude variations that might arise as a result of constitutional differences in the experimental subjects.

12. Peiser, A.: Beiträge zur Kenntnis des Stoffwechsels, besonders der Mineralien im Säuglingsalter: IV. Vergleichende Untersuchungen über den Stoffumsatz bei Ammenmilch und Eiweissmilch mit besonder Berücksichtung der Schwefelaushaltes, Jahrb. f. Kinderh. **81**:437, 1915.

13. Malmberg, N.: Ueber den Stoffwechsel des gesunden, natürlich ernährten Säuglings und dessen Beeinflussung durch parenterale Infektion und Intoxikation, Acta pædiat. **2**:209, 1923.

2. Individual twenty-four hour specimens have no value for metabolic investigations. Analysis of the average values for three consecutive twenty-four hour periods show distinct differences produced by change of diet.

3. The average intake of phosphorus with cow's milk was 0.654 Gm. per twenty-four hours and with breast milk 0.258 Gm. The total phosphorus output during the periods when cow's milk was used was almost four times as great as that during the periods when breast milk was given, namely, an average total output of 0.394 Gm. per twenty-four hours during the periods when cow's milk was used as compared to 0.108 Gm. during the periods when breast milk was fed. The increased output when cow's milk was used is due to a great extent to the increased phosphorus intake during these periods.

4. The average excretion of phosphorus in the urine was 0.275 Gm. per twenty-four hours during the periods of cow's milk feedings and 0.064 Gm. when breast milk was fed. The average value for phosphorus excreted in the feces was 0.119 Gm. per twenty-four hours for cow's milk and 0.044 Gm. for breast milk.

5. The actual quantities of phosphorus absorbed by the infants studied are considerably larger during the periods of cow's milk feeding, the average value for cow's milk being 0.535 Gm. per twenty-four hours compared to 0.213 Gm. for breast milk. However, the average percentage absorption for breast milk is 83.1 per cent as compared to 81.1 per cent for cow's milk.

6. The actual amounts of phosphorus retained were considerably greater during the periods when cow's milk was used, possibly as the result of a greater intake; for this reason it is difficult to compare the percentage values for retentions. However, over 50 per cent of the phosphorus intake was retained by each infant during the periods when it was breast fed, the values ranging from 51 to 63.8 per cent, with an average of 58.1 per cent. During the periods when cow's milk feedings were given, the retention was always below 50 per cent, the maximum being 44.2 per cent and the minimum, 29.2 per cent.

7. The values per kilogram obtained during the periods when the infant was breast fed indicate that the optimal absorption and retention of the phosphorus in breast milk occur in the earliest months of life.

THE DIAGNOSIS OF CONGENITAL SYPHILIS IN THE NEW-BORN *

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It has been the generally accepted plan in many clinics to regard as syphilitic those infants who are born of mothers known to be syphilitic, especially if the infant's Wassermann reaction is positive. This tradition has held in spite of a considerable amount of evidence that has been accumulated to show that an infant born of a mother with a positive Wassermann reaction is not necessarily infected with syphilis even if the Wassermann reaction of the infant's blood is positive.

Williams,[1] in 1920, stated that "the existence of a positive Wassermann on the part of the mother does not necessarily mean that her child will develop syphilis." Cruickshank [2] and Jeans and Cooke [3] came to a similar conclusion when, on reexamination of infants who at birth had positive Wassermann reactions, they found some whose blood gave a negative reaction although they had not received antisyphilitic treatment. Lemež [4] studied the Wassermann reaction in the first days of life and concluded that "healthy new-born infants of syphilitic mothers who show a transitory positive Wassermann reaction in the first two weeks of life are nevertheless to be considered as born free from syphilis so long as they continuously remain clinically healthy and Wassermann-negative." Cooke,[5] in studying the transference of the antibodies from mother to infant in tuberculosis, said that "a similar transference of complement-fixing substances from mother to infant has been noted in non-syphilitic children of syphilitic mothers." A positive Wassermann reaction on the cord blood and on the infant's blood in the first few days or weeks after birth may be due in some

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* From the United States Children's Bureau (Studies of Neonatal Morbidity and Mortality) and the Pediatric Department of the Yale School of Medicine.

1. Williams, J. W.: Bull. Johns Hopkins Hosp. **31**:335 (Oct.) 1920.

2. Cruickshank, J. N.: Medical Research Council, London, Special Report Series, no. 82, 1924, p. 19.

3. Jeans, P. C., and Cooke, J. V.: The Transmission of Syphilis to the Second Generation, Am. J. Syph. **6**:569 (Oct.) 1922.

4. Lemež, Leo: Die pseudopositive Wassermannsche Reaktion in den ersten Lebenstagen, Ztschr. f. Kinderh. **48**:97, 1929.

5. Cooke, J. V.: The Transmission of Complement-Fixing Substances from Mother to Child, Am. Rev. Tuberc. **6**:127 (April) 1922.

instances, not to actual infection of the infant but to antibodies passing from the mother's blood through the placenta into the infant's circulation.

If only one Wassermann test is done on such an infant's blood and is found positive, or if the proper evaluation is not given to repeatedly positive but weakening Wassermann reactions, these infants may bear unnecessarily the stigma of a diagnosis of syphilis and may be unnecessarily treated. If the cases of these infants are reported as cured cases of congenital syphilis because the Wassermann reactions of the blood have become negative after the use of antisyphilitic treatment, a false impression of the ease with which syphilitic infants are rendered Wassermann-negative will be given. In order to avoid unnecessary treatment and false conclusions with regard to the efficacy of treatment, it is important to differentiate between the cases of true congenital syphilis and those with a pseudopositive Wassermann reaction. Evidence that the Wassermann reaction on repeated tests during the neonatal period is weakening has proved to be the greatest help in thus differentiating between a real and a pseudopositive reaction.

Certain criteria have been used in the pediatric clinic of the New Haven Hospital and Dispensary for determining whether or not the new-born infant of a syphilitic mother should be treated for congenital syphilis and for interpreting the infant's Wassermann reaction.

The infant has always been regarded as syphilitic and treated when any signs of active syphilis were present regardless of the Wassermann reaction, or when, in the absence of clinical syphilis in the infant, the mother had an active or a recent syphilitic infection and had not received treatment.

Treatment of an infant whose mother had a positive Wassermann reaction has been withheld if the mother has had antisyphilitic treatment during pregnancy, even though the treatment was considered inadequate or had been given in the latter part of pregnancy. Treatment of the infant was also withheld in those cases in which the mother had latent syphilis; in those in which the mother had had treatment in a previous pregnancy, and in those in which the mother, though known to have been infected during or before a previous pregnancy, had already given birth to a nonsyphilitic infant since the date of her infection. Under these conditions treatment of the infant who himself is free from symptoms or signs has been withheld, regardless of his first Wassermann reaction, until the test could be repeated one or more times and evidence obtained with regard to change in the strength of the reaction. A proper evaluation of the tests may thus be made and a correct diagnosis established.

In all such cases in which treatment has not been given, the infant has been kept under close observation for the possible development of early signs of syphilitic infection.

A Wassermann test of the blood is made a day or two after birth. If the test is positive, it is repeated in a few days and again before discharge from the hospital at 10 days or 2 weeks of age. If on the second test the Wassermann reaction remains positive but is weaker, treatment is still withheld. At the third test the reaction will usually have become still weaker or even negative if the infant has not been infected with syphilis, and treatment may still be withheld. In those cases in which the second test does not show a weaker reaction than the first and does not become still weaker at the end of ten days, the infant is regarded as syphilitic and treatment is begun. It is probable from reports in the literature that the period of observation may even be extended beyond ten days in carefully selected cases if the mother is willing to cooperate and bring the infant for frequent repetition of the test. It can be explained to the parents that repeated tests are better than prolonged treatment. There is some evidence that the antibodies transferred from the mother may persist in the infant's blood for several weeks. If any evidences of syphilis appear, by either physical or roentgenographic examination, treatment is begun regardless of changes in the Wassermann reaction.

OBSERVATIONS ON INFANTS

A group of fourteen such infants of syphilitic mothers has been studied, and, in spite of positive Wassermann reactions,[6] treatment has been withheld according to the criteria outlined. Table 1 shows the parity, Wassermann reactions and treatment of the mothers. The results of the Wassermann reactions in the infants are shown in table 2. All of these infants were under observation from birth. None of them showed clinical evidences of syphilis at birth, although three had palpable spleens and two had slight transient snuffles.

Roentgenograms of the long bones were normal in the seven cases in which they were taken within the first ten days after birth. Spinal punctures were not done during the early period of observation.

The Wassermann reaction showed at the first test complete fixation (both antigens) in three cases and a weaker reaction in eleven cases. Usually a weaker reaction was seen at the second or third test, and then a negative reaction. A negative or weaker reaction was usually obtained before the infant left the hospital (from ten days to two weeks). All of

6. At the time this study was made the Wassermann was the routine test used. The cholesterolized antigen used was extremely sensitive. Later the Kahn test was done and is reported in some of the cases.

TABLE 1.—*Wassermann Tests* (Mothers)*

No.	Name	Number of Previous Pregnancies	Wassermann Reaction	Treatment
1	R. L.	1	4+	Begun 3 years previously and continued through second pregnancy
2	M. H.	7	4+	None for 1 year; irregular treatments for 4 years previously
3	N. L.	0	4+	Treatment for 2 months prior to delivery
4	M. E.	10	2+	One treatment 4 months before delivery of eleventh child; treated fourteen times 3 years previously
5	F. P.	10	4+	None
6	R. P.	3	Negative in 1925	Five treatments during last month before delivery; several courses previously
7	A. M.	1	+	Five times during second pregnancy
8	A. D'O.	11	4+	None
9	L. I.	0	4+	Three times 4 years previously
10	E. G.	7	3+	Treated several times 2 years previously
11	E. G.	8	Negative	Treated several times
12	A. F.	0	4+	Six times during pregnancy
13	L. J.	0	4+	None
14	M. DR.	14	4+	Nineteen times during fifteenth pregnancy

* Reaction to alcoholic antigen.

TABLE 2.—*Wassermann and Kahn Tests* (Infants)*

			Days													Months											Years		
No.	Name	Cord	1	2	3	4	5	6	7	8	9	10	11	12	13	14	1	2	3	4	5	6	7	8	9	10	11	12	2	3	4
1	S. L.	..	..	..	..	0	..	..	..	..	..	..	..	..	..	..	0	..	..	0	..	..	0	..	..	..	..	0	..	0	..
						4											0			0			0					0		0	
2	E. H.	..	0	..	..	..	..	..	..	..	..	..	..	..	..	..	..	0	..	..	..	..	..	0	..	..	..	..	..	..	0	..
			4															0						0						0	
3	R. L.	2	..	..	..	..	..	..	..	..	..	..	..	..	..	..	0	0	..	..	..	..	..	..	..	0	..	..	0	0	0	0
		4															4	0								0			0	0	0	0
4	M. E.	..	0	..	..	..	..	..	..	0	..	..	..	..	..	..	0	..	..	0	..	..	..	..	..	..	..	..	..	..	..	..
			3							0							0			0											
5	M. P.	4	..	K	..	..	..	..	..	..	..	..	..	..	4	..	..	..	..	0	..	..	..	..	..	..	..	..	..	..	..	..
		4		4											4					0											
6	K. P.	..	..	..	4	..	..	..	..	..	..	0	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	0	..	..	..
					4							0																0			
7	E. M.	2	..	..	..	..	..	..	..	..	..	..	..	..	..	..	0	..	..	..	..	0	..	..	..	..	..	..	0	..	..	
																	4					0							0		
8	W. D'O.	0	..	..	..	..	..	..	..	..	..	..	..	..	..	0	..	0	..	..	..	..	..	..	..	..	..	..	..	..	..	..
		4														0		0														
9	I.	..	..	..	4	..	..	..	..	..	..	0	..	..	..	0	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
					4							1				0																
10	R. G.	3	..	..	..	..	K	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	0	..	..	..
							3																					0			
11	E. G.	..	0	..	..	..	..	..	..	..	..	..	..	..	..	K	..	..	..	0	K	..	..	..	K	..	..	..	..	..	..	..
			4													0				0	0				0							
12	J. F.	..	..	..	..	..	..	1	..	..	..	..	..	..	..	..	0	..	..	..	K	..	..	..	..	..	..	..	..	..	..	..
								4									0				0											
13	J. J.	3	..	..	..	..	..	..	..	..	..	..	..	..	..	..	0	..	..	..	..	..	..	..	K	..	..	..	..	..	..	..
																	0								0							
14	M. D'R.	0	..	0	..	..	..	..	..	..	..	..	..	..	..	..	0	0	0	..	0	..	..	..	..	..	..	..	..	..	..	..
		3		0													0	0	0		0											

* When two figures are given, the upper figure refers to the reaction of the alcoholic antigen, the lower to the reaction of the cholesterinized antigen as 1, 2, 3 or 4 plus. When K appears over a figure, the K refers to the Kahn and the figure refers to the reaction as 1, 2, 3 or 4 plus. When one figure appears alone, this figure refers to the reaction with the Kolmer technic.

the infants have continued to have negative reactions during the period of observation. None of them has received any antisyphilitic treatment. None of the infants has developed any clinical evidence of syphilis. It is our belief that these infants were probably not syphilitic, and that treatment, if instituted, would have been carried out unnecessarily.

The longest period of observation for any child in the series was four years, and the shortest, two months. Jeans and Cooke [8] stated in their study that they had never encountered the appearance of the infection in an infant whose Wassermann reaction was negative at 2 months of age. One premature infant included in the series died at the age of 39 days. No evidences of syphilis were found clinically or at postmortem examination. The remaining thirteen infants were well at the time the last Wassermann test was made.

CONCLUSIONS

It may be concluded that in suitable cases in which the Wassermann reaction of the mother's blood is positive, repetition of the Wassermann test on the new-born infant at frequent intervals will aid in differentiating between reactions that indicate a true syphilitic infection and those that are positive because of the passage of antibodies from the mother to the infant. Correct evaluation of the results of repeated tests will prevent the unnecessary treatment of nonsyphilitic infants.

EXCRETION OF CREATINE AND CREATININE

HOURLY EXCRETION IN NORMAL CHILDREN AND IN CHILDREN WITH PROGRESSIVE MUSCULAR DYSTROPHY *

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During studies on creatine and creatinine metabolism, the hourly excretion of these substances was determined in two cases of muscular dystrophy, one case of chronic anterior poliomyelitis and in two normal boys.

Shaffer [1] found that the excretion of creatinine was constant throughout a twenty-four hour period as well as from day to day. Since that time cases have been studied which show that this constancy is not always found. Fluctuation in creatinine output during short fasts was noted by Neuwirth.[2] Schultz [3] found periodic variations in creatinine excretion during the day, irrespective of diet or sleep. Definite increases occurred at from 9 to 11 a. m., 3 to 5 p. m. and 9 to 11 p. m. He found the creatinine output at night to be slightly less than that during the day. Simpson [4] considered the urine volume to be a factor in variations in the creatinine excretion observed during a twenty-four hour period.

In my studies [5] a comparison was made of the urine volume, creatine and creatinine excretion at hourly intervals during the day (7 a. m. to 5 p. m.) and of the pooled specimens from 5 p. m. until 7 a. m. The patients were maintained on a diet free from meat or meat stock for the duration of the experiment and for at least four days previously. Creatinine was determined by the method of Folin,[6] and his picric acid method was used for the estimation of creatine.

Brief histories are given in the aforementioned paper for case 1, severe muscular dystrophy, and case 2, a mild form of the same disease.

CASE 3.—A white boy, aged 10, had a case of residual poliomyelitis of the right leg and chronic osteomyelitis of the right femur. Poliomyelitis occurred in 1924, with paralysis of both legs and residual partial paralysis of the right leg. Osteomyelitis developed in 1925. The patient was admitted to the

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hospital on Aug. 14, 1930, for a new brace and to correct a flexion deformity of the right hip. When discharged (October 21) he was able to walk with a brace for the right leg. The left leg was normal. There was loss of action of the flexors and partial loss of action of the extensors of the right foot, the peroneal, the anterior and posterior tibial and the gastrocnemius muscles of the right leg. The majority of the muscles of the right thigh and hip were also impaired: the gluteus maximus, hip flexors, abductors, adductors, the quadriceps and the hamstrings. Other physical findings were normal.

TABLE 1.—*Hourly Excretion of Creatine and Creatinine in Case 1, Muscular Dystrophy*

	October 13 Normal Day			October 29 Normal Day			October 30 Fasting Until 12 Noon		
Time	Urine Volume, Cc.	Creatinine, Mg.	Creatine as Creatinine, Mg.	Urine Volume, Cc.	Creatinine, Mg.	Creatine as Creatinine, Mg.	Urine Volume, Cc.	Creatinine, Mg.	Creatine as Creatinine, Mg.
8 a.m.	93	20.4	15.1	55	5.3	12.5	103	13.3	24.2
9 a.m.	30	7.8	9.9	78	6.1	17.9	35	4.5	9.4
10 a.m.	27	4.0	9.0	270	8.5	30.0	355	5.5	22.1
11 a.m.	50	31.2	21.6	278	8.1	27.0	360	6.0	18.7
12 m.	...	....	....	260	6.3	23.0	124	5.1	15.7
1 p.m.	170	12.6	44.4	43	5.5	17.2	28	1.5	4.1
2 p.m.	115	3.2	7.0	112	9.3	25.5	24	1.8	3.0
3 p.m.	20	3.5	7.5	88	1.7	6.0	50	1.4	3.8
4 p.m.	285	7.5	19.5	335	5.9	17.9	180	11.1	21.9
5 p.m.	...	....	....	240	7.0	15.2	145	7.2	12.4
4 p.m.–7 a.m.	430	44.0	50.0						
5 p.m.–7 a.m.	...	....	....	250	80.0	72.0	165	66.4	93.6
Total	1,220	134.2	193.0	2,009	143.7	264.2	1,578	123.8	228.8

	Dextrose Administration—October 24 1.75 Gm. Dextrose per Kilogram of Body Weight at 8 a.m.			Dextrose Administration—October 16 1.75 Gm. Dextrose per Kilogram of Body Weight at 8 a.m.			
Time	Urine Volume, Cc.	Creatinine, Mg.	Creatine as Creatinine, Mg.	Time	Urine Volume, Cc.	Creatinine, Mg.	Creatine as Creatinine, Mg.
8:30 a.m.	43	14.4	5.0	8 a.m.	60	8.9	16.3
9:30 a.m.	62	9.5	15.0	9:10 a.m.	30	5.5	14.5
10:30 a.m.	270	7.9	24.6	9:40 a.m.	30	3.5	14.7
11:30 a.m.	225	8.5	26.7	10:40 a.m.	310	6.9	29.8
12:30 p.m.	235	6.7	10.2	11:40 a.m.	345	6.9	22.1
1:30 p.m.	210	8.1	11.9	12:40 p.m.	100	6.3	15.9
2:30 p.m.	163	5.3	8.9	1:40 p.m.	250	6.4	22.3
3:30 p.m.	75	7.5	15.9	2:40 p.m.	180	7.8	24.4
4:30 p.m.	273	3.8	10.6	3:40 p.m.	220	5.8	16.2
5:30 p.m.	370	5.5	17.2	4:40 p.m.	250	6.1	16.5
5:30 p.m.–7 a.m.	585	48.5	48.5	4:40 p.m.–7 a.m.	350	56.0	100.0
Total	2,511	125.7	194.0	Total	2,105	120.1	292.8

The subject in case 4 was a normal boy, 9 years of age, and the subject in case 5 was a normal boy, 6 years of age.

A definite variation in creatinine excretion with a more marked fluctuation in creatine is observed. In a few instances these fluctuations may be correlated with the changes in urine volume, but this is by no means a constant finding.

The hourly excretion in case 1 for six days is indicated in table 1. It can be seen that irrespective of the diet, whether breakfast was omitted, whether 1.75 Gm. of dextrose per kilogram of body weight for a dextrose tolerance test was substituted for the morning meal or whether

the usual regimen was maintained, definite fluctuations occurred in the creatine and creatinine excretion. In this case the increase in these substances occurred at the same time on almost every day. On two of the days studied the correlation of the creatine and creatinine excretion with the urine volume is striking. On October 16 and 24 there was the same

TABLE 2.—*Hourly Excretion of Creatine and Creatinine in Case 2, Muscular Dystrophy*

Normal Day December 4				Normal Day December 26				Fasting Until 12 Noon December 28			
Time	Urine Volume, Cc.	Creatinine, Mg.	Creatine as Creatinine, Mg.	Time	Urine Volume, Cc.	Creatinine, Mg.	Creatine as Creatinine, Mg.	Time	Urine Volume, Cc.	Creatinine, Mg.	Creatine as Creatinine, Mg.
a.m.				a.m.				a.m.			
8	87	58	16	8:30	290	114	35	7	295	59.5	18.5
9	48	23.9	25.8	9:30	44	29.2	9.8	8	265	42	17.5
10	405	27.7	29.7	10	188	19.1	11.2	9	215	14.8	4
11	205	25.6	22.7	11:30	350	21.9	7.1	10	355	23	2.8
12	252	22	16.7	12:30	111	28.5	0	11	80	26.6	0
p.m.				p.m.				12	120	19	5.4
1	98	23	17.7	1:30	150	19.1	4.1	p.m.			
2	363	24.8	18.2	2:30	120	22.2	1.8	1	60	25	12
3	285	24.8	10.8	3:30	165	8	4.3	2	95	23.8	6
4	340	23.2	6.3	4:30	290	32.2	0	3	40	29.6	0
5	252	21	7.9	4:30–				4	108	22	3.4
6	155	22	7.4	7 a.m.	750	220	0				
7	130	18.8	6.8								
9	160	13.3	5	Total	2,458	514.2	73.3				
6 a.m.	460	180	2								
Total	3,240	508	190								

Dextrose Administration—December 5 1.75 Gm. Dextrose per Kilogram of Body Weight at 8 a.m.				Dextrose Administration—December 8 1.75 Gm. Dextrose per Kilogram of Body Weight at 8 a.m.			
Time	Urine Volume, Cc.	Creatinine, Mg.	Creatine as Creatinine, Mg.	Time	Urine Volume, Cc.	Creatinine, Mg.	Creatine as Creatinine, Mg.
7:30 a.m.	80	43.3	7.4	7:30 a.m.	360	96	34
8:00 a.m.	20	13.3	1.4	8:30 a.m.	56	28	6
9:30 a.m.	225	22.4	8.6	9:30 a.m.	420	21.6	10.8
10:30 a.m.	483	22.4	6	10:30 a.m.	465	15.5	7.7
11:30 a.m.	168	21	7	11:30 a.m.	205	20.5	4.1
12:30 p.m.	155	19.4	3	12:30 p.m.	73	18.3	6.1
1:30 p.m.	165	20.6	16.1	1:30 p.m.	300	25	11.3
2:30 p.m.	192	22.2	11.8	2:30 p.m.	148	26.9	4.3
3:30 p.m.	223	22.5	14.7	3:30 p.m.	248	25.8	9.7
4:30 p.m.	250	15.6	7.1	4:30 p.m.	250	23.8	8.2
5:30 p.m.	160	18.8	5.8	7:30 p.m.	258	25.8	55
6:30 p.m.	273	31.2	10.8	7:30 p.m.–6 a.m.	600	250	0
6:30 p.m.–6 a.m.	420	220	0				
Total	2,614	492	100	Total	3,383	577.2	107.7

correlation in the morning specimens but not in those of the afternoon. With the exception of October 24, a definite increase in creatine and creatinine was observed every day at from 10 to 11 a. m. The increases in the afternoon were not as constant, occurring from 2 to 4 p. m. On three days (October 16, 24 and 30) the maximum excretion of creatinine occurred at from 8 to 8:30 a. m. During the period of study of this case, the creatinine excretion exceeded that of the creatine only twice (11 a. m., October 13 and 8:30 a. m., October 24). The creatinine

from 5 p. m. to 7 a. m. varied from 22 to 55 per cent, indicating less excretion during the night. The percentage of creatine eliminated during the night was at an even lower level, from 21 to 34.

The fluctuations in creatinine excretion in case 2 (table 2) were not as marked as in case 1, nor did the variations occur as regularly with those of the creatine excretion. During the day the largest amount of creatinine was excreted consistently between 7:30 and 8 a. m.

TABLE 3.—*Hourly Excretion of Creatine and Creatinine*

Case 3 Chronic Anterior Poliomyelitis — Time	Normal Day October 17 — Urine Volume, Cc.	Creatinine, Mg.	Creatine as Creatinine, Mg.	1.75 Gm. Dextrose per Kilogram of Body Weight at 8 a.m., October 20 — Urine Volume, Cc.	Creatinine, Mg.	Creatine as Creatinine, Mg.
8 a.m.	155	38.8	9.7	42	41	2.8
9 a.m.	160	13.3	17.3	208	24.5	20.1
10 a.m.	200	9.3	10.7	170	14.3	8.8
11 a.m.	270	20.7	14.3	405	18.7	15.2
12 m.	290	19.3	14.7	200	12.3	8.2
1 p.m.	90	13.2	8	215	19.3	6.1
2 p.m.	...	....	....	115	15.3	7.1
3 p.m.	185	13.8	9.3	120	21.8	15.2
4 p.m.	300	17	14.5	30	13	4.1
5 p.m.	200	18.2	1			
4 p.m.–7 a.m.	...	....	....	595	190	4
5 p.m.–7 a.m.	535	157	55			
Total	2,385	320.6	154.5	2,100	370.2	91.6

Case 4, Normal Child of 9 Years Normal Day—November 10 — Time	Urine Volume, Cc.	Creatinine, Mg.	Creatine as Creatinine, Mg.	Case 5, Normal Child of 6 Years Normal Day—November 5 — Time	Urine Volume, Cc.	Creatinine, Mg.	Creatine as Creatinine, Mg.
8 a.m.	75	80	2	8:30 a.m.	91	36	23
9 a.m.	180	28	2.2	10:00 a.m.	125	11.2	7.3
10 a.m.	200	14.3	0	11:00 a.m.	520	20.6	10
11 a.m.	420	42	3	12:00 m.	440	17.6	8.2
12 m.	...	....	....	12:30 p.m.	370	13.4	7.9
1 p.m.	175	30.4	3.2	1:30 p.m.	136	7.4	3.5
2 p.m.	240	38.4	2.2	2:00 p.m.	66	20.6	5.4
3 p.m.	140	28	5	3:30 p.m.	135	13.4	5.9
4 p.m.	245	22.2	2	4:15 p.m.	99	14.2	5.6
5 p.m.	250	16.5	0	5:15 p.m.	150	7.2	4.9
6 p.m.	330	40.4	4.9	6:45 p.m.	115	27.6	10.6
6 p.m.–7 a.m.	260	195	13	6:45 p.m.–7 a.m.	1,200	165.9	35.4
Total	2,415	535.2	37.5	Total	3,547	355.1	128.1

Other increases during the day occurred at irregular intervals. The creatinine excretion from 5 p. m. to 7 a. m. varied from 43 to 51 per cent, indicating that slightly less than half was excreted at night. The variations in the hourly excretion of creatine were much more marked than those of the creatinine. With the exception of the day when no breakfast was given, there was a definite maximum excretion every morning at 10 a. m. On three days, there were afternoon peaks at 1:30 and 3:30; on the other two days (December 4 and 28), there was a decided reduction at 3 p. m. The amount of creatine eliminated from 5 p. m. to 7 a. m. varied from 0 to 16 per cent. There is no correlation

between the creatine and creatinine excretion and the urine volume in this case.

On the two days studied in case 3 (table 3), chronic anterior poliomyelitis (with paralysis of only the right leg), the creatinine excretion was rather variable, definite increases occurring at 8 and 11 a. m. and at 3 and 4 p. m. Half of the total creatinine was excreted from 5 p. m. to 7 a. m. The excretion of creatine varied directly with that of the creatinine in the majority of the specimens. Two increases in creatine were observed in the morning, at 9 and 11 a. m., and there was one afternoon peak at 3 or 4 p. m. The excretion from 5 p. m. to 7 a. m. was 36 per cent on one day and 4 per cent on the other. The urine volume bears some relation to the creatine and creatinine excretion, but it is not as marked as in case 1.

The two normal boys, cases 4 and 5 (table 3), showed the same fluctuation in creatine and creatinine excretion. An increase in the creatinine excretion in these normal cases occurred at 8 and 11 a. m., and at 3 p. m. in case 4. Case 5 showed only the morning peaks at 8 and 11 a. m. The creatine excretion during the night in case 4 (36 per cent) was less than that during the day, but in case 5, it was approximately half of the total excretion (47 per cent). The correlation of urine output and creatine and creatinine excretion is not marked.

SUMMARY

The hourly excretion of creatine and creatinine in the five cases studied shows a marked fluctuation of both substances. In some instances the fluctuations are related to variations in urine volume. This is more marked in case 1, which shows an abnormal creatine and creatinine metabolism. The creatinine coefficient, 2, was very low and the total creatinine coefficient, 6, was below normal. This is characteristic of muscular dystrophy. There is no correlation in urine volume and creatine and creatinine excretion in case 2, a mild dystrophic condition in which there was a low normal creatinine and total creatinine coefficient (5.9 and 7.1).[5] There was little correlation of urine volume and creatine and creatinine excretion in the case of chronic anterior poliomyelitis and in the two normal subjects.

Although individual cases show a maximum excretion of creatine and creatinine at definite hours of the day, variation from case to case is too marked to conclude that the fluctuations occur at definite intervals. There is no definite correlation in simultaneous maximum excretion of creatine and creatinine, although in some cases it was noted.

In every case there was a greater excretion of creatine and creatinine during the day than during the night. The higher percentage of creatine eliminated during the day may indicate a correlation between this substance and changes in metabolic activity.

BASAL METABOLISM OF NORMAL CHILDREN

THE PUBERTY REACTION *

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NEW YORK

In the past few years there have been many studies of the basal metabolism of children, and a useful set of charts has been published by Talbot [1] showing the normal standards for the metabolism of children. He stated, however, that "the metabolism during puberty will have to be studied further before any standards may be accepted."

The question of the basal metabolism just prior to, during and just after puberty has not been settled. Older investigators believed that there is a rise in basal metabolism in the prepubescent period. This belief was supported by DuBois [2] who made a study of the basal metabolism of some boy scouts just before puberty. These boys were again studied after puberty had been established,[3] and their metabolism had fallen from 25 to 11 per cent above that of adults. Benedict and Talbot [4] in a few observations at this period found no such increase, but they admitted that their experiences were not sufficient to warrant a definite conclusion. We quote Du Bois [5] who said: "Personally I believe that there is a rise in basal metabolism before puberty with a subsequent fall; but the proof will come only when a number of individual boys and girls are studied every year, or better, every six months between the ages of 10 and 16 years."

A study similar to that suggested by Du Bois has been in progress at this clinic for the past four years. The changing population of the neighborhood in which our hospital is located makes it increasingly

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1. Talbot, F.: Standards of Body Metabolism in Normal Infants and Children, Am. J. Dis. Child. **21**:519 (June) 1921.

2. Du Bois, E. F.: Clinical Calorimetry, Arch. Int. Med. **17**:887 (June) 1916.

3. Olmstead, W. H.; Barr, D. P., and Du Bois, E. F.: Clinical Calorimetry, Arch. Int. Med. **21**:621 (May) 1918.

4. Benedict, F. G., and Talbot, F.: Metabolism and Growth from Birth to Puberty, Washington, D. C., Carnegie Institution of Washington, 1921, publ. no. 302.

5. Du Bois, E. F.: Basal Metabolism in Health and Disease, Philadelphia, Lea & Febiger, 1927, p. 147.

difficult to continue this study, but the material collected in the past four years is of sufficient interest to publish in this paper.

The basal metabolism of thirty-eight children (twenty-eight girls and ten boys) between the ages of 10 and 16 years was studied at intervals of from six months to a year, for periods ranging from one to four years. The tests were all made in the postabsorptive state under the accepted standard conditions. The Krogh respirometer and later the Benedict-Roth apparatus were used. Every child had an initial practice test several days before the first recorded test, so as to eliminate nonbasal figures due to excitement or apprehension of the novel experience.

The table gives the data in all tests. The results are expressed as total calories per twenty-four hours. The percentage variation from a normal standard is calculated from the Pirquet sitting height standard,[6] which we find the best single prediction standard in all cases.

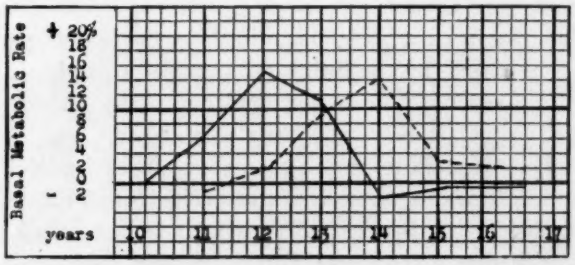

Chart 1.—Basal metabolic rate of normal boys and girls at different age periods. The solid line represents girls; the broken line, boys.

We find that this standard agrees closely with the Talbot standard[7] based on height alone, which Benedict[8] recommended for growing children. The Pirquet and Talbot standards are the only two that are not based on weight. The condition of nutrition of the children is expressed by the Pirquet pelidisi.[9] The average basal metabolism by age and sex is plotted as a curve in chart 1.

Chart 1 shows a definite increase in metabolism before and during early puberty, followed by a fall after puberty is established. This rise occurs at the ages of 12 to 13 years in the girls, at 13 to 14 years in the boys. This is consistent with the fact that girls attain puberty earlier than do boys. The average basal metabolism at 11 years of

6. Pirquet, C.: An Outline of the Pirquet System of Nutrition, Philadelphia, W. B. Saunders Company, 1922.

7. Talbot, F.: Physiol. Rev. **5**:477, 1925.

8. Benedict, F. G.: Am. Phil. Soc. **43**:25, 1924.

9. Pirquet, C.: System der Ernährung, Berlin, Julius Springer, 1919, pt. 2, p. 284.

age is higher in the girls than in the boys, probably because puberty has already begun in girls at this time. After puberty has been established in both the girls and boys, the average basal metabolism is somewhat lower in the former than in the latter, due probably to a lessened physical activity.

The increase in basal metabolism during pubescence occurs at different times in individual cases, and is coincident with the physiologic rather than with the chronological age. In those children in whom puberty begins earlier, the rise in metabolism begins earlier. Out of twenty-two girls in whom catamenia was established, eight or 36 per cent began to menstruate at the age of 12; thirteen or 60 per cent at the age of 13, and one or 4 per cent at the age of 14. The rise in the basal metabolism is parallel to this curve (chart 2). The duration of the increase in basal metabolism varied. We found an increase in metabolism from one to eight months before the onset of menstruation,

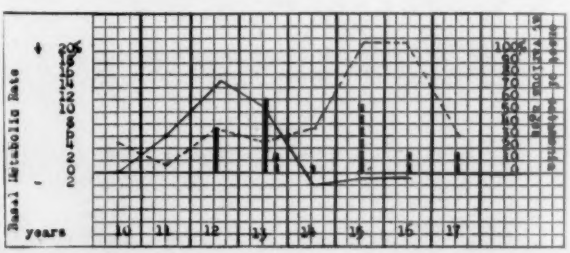

Chart 2.—Relationship between basal metabolic rate and onset of catamenia. The lines respresent the basal metabolic rate, the blocks represent the onset of catamenia at various ages, in per cent. The broken lines and blocks refer to a group of diabetic girls studied; the uninterrupted lines and blocks to the present series of normal girls.

and this increase was maintained from one to six months after the onset of menstruation. The height of the increased metabolism also varied with the individual case; there seemed to be no uniformity in the percentage of increase. Perhaps this will make it difficult to establish normal standards for the years between 11 and 14. We firmly believe that there is a prepuberty rise in basal metabolism, but this rise is individual and cannot be predicted from the preceding metabolic rate.

The pulse rate rose with the rise in metabolism and fell coincidentally with the return of the metabolic rate to normal. In several cases (nos. 5, 8, 13, 23 and 27) electrocardiographs registered a pronounced tachycardia. In two of these case (nos. 5 and 23) a systolic murmur led to a suspicion of an organic lesion. In all these cases, however, except case 23, the murmur disappeared, and the pulse rate became normal after menstruation was established. In case 23, menstruation had not been established; the murmur and the tachycardia still persisted.

Basal Metabolism of Children: The Puberty Reaction
Girls

Case	Date of Test	Age		Height, Cm.	Sitting Height, Cm.	Weight, Kg.	Pelidisi	Pulse Rate	Heat Production: Total Calories per 24 Hours			Comment
		Years	Months						Obtained	Predicted	Per Cent Variation	
1 (O. F.)	5/10/26	12	..	148	78	49.6	102	64	1,096	1,197	— 8	Simple goiter; menses at 12 years, 10 months
	5/16/27	13	..	154	80	48.9	90	80	1,438	1,280	+13	
	6/25/28	14	1	158	83	56	100	66	1,380	1,377	0	
	9/17/29	15	4	160	84	57	99	64	1,340	1,411	— 5	
	8/ 7/30	16	3	163	87	61	98	68	1,483	1,513	— 2	
2 (M. C.)	5/12/27	12	3	143	73	33	95	80	1,128	1,065	+ 6	
	6/15/28	13	4	153	80	43	95	90	1,580	1,280	+23	Menses at 13 years, 5 months
	12/ 7/29	14	6	153	80	46.6	97	72	1,272	1,280	0	
	5/ 2/30	15	3	154	81	46	96	72	1,320	1,312	0	
	2/ 7/31	16	..	155	81	48.7	97	74	1,296	1,312	— 1	
3 (B. O.)	1/ 8/27	12	..	142	77	41	97	90	1,248	1,185	+ 6	
	12/24/27	12	11	150	80	46	97	100	1,490	1,280	+17	Menses at 13 years, 3 months
	12/ 2/28	13	11	156	85	55	97	76	1,440	1,445	0	
	3/ 2/29	14	2	157	86	58.6	98	80	1,388	1,478	— 6	
	12/30/29	14	11	158	86	60.3	99	84	1,529	1,479	+ 3	
	6/30/30	15	4	160	87	63	99	82	1,600	1,513	+ 6	
	1/16/31	16	..	160	81	63.4	99	72	1,530	1,513	0	
4 (A. M.)	6/11/28	13	4	148	80	41	94	76	1,245	1,280	— 3	
	3/21/29	14	1	155	81	44	94	110	1,560	1,312	+19	Menses at 14 years, 2 months
	10/19/29	14	8	160	84	50	95	80	1,514	1,411	+ 7	
	5/24/30	15	3	161	84	51	96	78	1,400	1,411	0	
	2/ 2/31	16	..	161	84	52	96	72	1,417	1,411	0	
5 (F. G.)	6/28/27	12	9	151	80	37	90	80	1,216	1,280	— 5	Simple goiter; tremor, tachycardia; functional murmur; nervousness; menses at 13 years, 10 months; no symptoms afterward
	5/11/28	13	8	159	82	38.9	90	108	1,572	1,345	+17	
	4/ 4/29	14	6	162	86	39.8	86	76	1,420	1,479	— 4	
	11/19/29	15	2	163	87	42	86	76	1,440	1,479	— 2	
	1/11/31	16	4	165	88	46	88	72	1,473	1,549	— 5	
6 (B. L.)	12/28/27	12	3	146	78	35	90	90	1,488	1,217	+22	Nervous; menses at 13 years
	3/23/29	13	6	156	81	41	92	84	1,490	1,312	+14	
	12/ 7/29	14	3	162	84	45	92	78	1,372	1,411	— 3	
	5/16/30	14	8	168	86	50	93	80	1,400	1,479	— 5	
	1/14/31	15	4	163	88	55	94	80	1,600	1,549	+ 3	
7 (J. C.)	11/24/26	11	8	146	79	33.5	88	70	1,214	1,248	— 3	
	12/19/28	12	9	155	82	39.5	90	88	1,510	1,345	+13	Menses at 12 years, 10 months
	6/19/29	13	4	158	85	43.5	91	78	1,416	1,445	— 2	
	12/10/29	13	9	164	86	45.6	90	66	1,472	1,479	0	
	5/15/30	14	2	165	87	49	91	76	1,508	1,513	0	
	2/ 2/31	15	..	166	88	50.5	91	72	1,580	1,549	+ 2	

8 (J. B.)	2/14/28	12	6	150	78	49.8	102	100	1,500	1,217	+23	Tachycardia; simple goiter; nervousness; tremor; no symptoms now; menses at 13 years
	3/23/29	13	7	155	83	56	100	80	1,440	1,377	+ 5	
	7/17/30	15	..	159	84	58.5	100	72	1,320	1,411	— 6	
9 (P. N.)	2/ 8/30	13	1	161	82	40.9	91	110	1,513	1,345	+13	Rapid growth in past year; menses at 13 years, 3 months
	8/ 9/30	13	7	165	86	50.3	93	80	1,440	1,479	— 2	
	1/19/31	14	..	167	86	50.5	93	74	1,538	1,479	+ 4	
10 (H. Z.)	1/27/27	12	..	157	86	79	108	90	1,800	1,479	+22	
	7/28/28	13	6	162	87	78	106	80	1,704	1,513	+13	Menses at 13 years
	1/22/29	14	..	162	88	78	106	80	1,702	1,549	+ 9	
11 (A. J.)	9/19/27	10	8	135	70	27	93	68	904	980	— 8	Simple goiter; menses at 12 years, 9 months
	7/16/29	12	6	147	77	36	93	80	1,390	1,185	+18	
	11/24/29	12	11	149	77	35.5	93	74	1,290	1,185	+ 9	
	6/10/30	13	5	150	79	40	94	68	1,258	1,248	0	
	1/10/31	14	..	153	80	41	94	69	1,200	1,280	— 7	
12 (M. T.)	5/ 7/27	11	9	145	74	49	107	76	1,180	1,095	+ 8	
	7/ 7/28	12	11	160	82	67	107	88	1,536	1,345	+15	
	7/ 9/29	13	11	163	83	65.8	105	78	1,445	1,377	+ 5	Menses at 13 years, 1 month
	2/28/31	14	6	168	85	70	105	78	1,530	1,445	+ 6	
13 (M. K.)	12/ 2/28	11	3	138	73	32.4	95	80	1,120	1,065	+ 5	
	6/27/29	11	9	142	77	38	95	90	1,392	1,185	+18	Flushes; tachycardia; nervousness; menses at 12 years, 5 months
	12/21/29	12	3	145	78	41	96	100	1,512	1,217	+24	
	5/27/30	12	8	150	79	43	96	88	1,312	1,248	+ 5	
	10/16/30	13	1	150	81	46.5	96	76	1,248	1,312	— 5	No symptoms now
	3/ 7/31	13	6	150	81	47	96	72	1,380	1,312	+ 5	
14 (E. M.)	5/13/28	10	..	139	75	45.4	103	80	1,205	1,125	+ 7	
	8/22/29	11	3	142	76	53.2	107	88	1,359	1,155	+18	
	8/28/30	12	3	152	83	61.6	103	78	1,464	1,377	+ 5	Menses at 12 years, 1 month
15 (S. G.)	5/17/28	11	6	143	77	57	108	88	1,353	1,185	+15	
	5/31/30	13	6	157	86	70.5	104	80	1,584	1,479	+ 7	Menses at 12 years, 11 months
16 (R. M.)	11/ 8/30	11	3	149	76	35	94	82	1,284	1,155	+ 9	Rapid growth past year; no menses as yet
	7/26/30	11	11	154	77	37.7	94	80	1,296	1,185	+ 9	
	12/20/30	12	4	156	77	41	97	90	1,392	1,185	+18	
17 (B. S.)	2/10/29	11	1	139	72	29	92	70	1,008	1,037	— 2	
	1/ 8/30	12	..	149	76	34	92	90	1,400	1,155	+21	Simple goiter; nervousness; menses at 12 years, 8 months
	1/15/31	13	..	154	80	41	94	72	1,300	1,280	+ 2	
18 (J. S.)	11/17/28	11	3	148	76	48	103	70	1,152	1,155	0	
	3/ 2/29	11	7	150	77	49	103	76	1,272	1,185	+ 8	
	4/19/30	12	8	157	79	50	101	82	1,392	1,248	+12	No menses
19 (R. A.)	1/ 3/29	11	1	145	76	50.5	105	80	1,224	1,155	+ 6	
	2/ 6/30	12	2	150	79	50	101	78	1,392	1,248	+11	Simple goiter since 2 months of age; no menses as yet
	1/31/31	13	1	156	80	50	100	88	1,512	1,280	+18	

Basal Metabolism of Children: The Puberty Reaction—Continued

Girls

Case	Date of Test	Age		Height, Cm.	Sitting Height, Cm.	Weight, Kg.	Pelidisi	Pulse Rate	Heat Production: Total Calories per 24 Hours			Comment
		Years	Months						Obtained	Predicted	Per Cent Variation	
20 (E. S.)	12/13/29	12	3	156	83	50	96	80	1,580	1,377	+15	Menses at 12 years, 6 months
	5/17/30	12	8	159	86	59	98	86	1,576	1,479	+ 7	
	11/16/30	13	2	160	86	59	98	76	1,512	1,479	+ 2	
21 (I. A.)	12/22/29	12	..	140	78	30.4	87	66	1,128	1,217	— 7	
	5/ 8/30	12	5	144	80	36.5	90	84	1,404	1,280	+10	
	12/24/30	13	..	146	82	41	91	90	1,536	1,345	+14	Menses at 13 years, 1 month
	3/ 7/31	13	3	148	82	42	92	70	1,300	1,345	— 3	
22 (S. V.)	1/23/29	11	11	136	72	31.5	95	76	1,100	1,037	+ 6	
	7/12/30	12	5	142	73	33	95	88	1,272	1,065	+19	
	12/13/30	12	10	142	74	35	96	86	1,280	1,095	+18	No menses
23 (S. S.)	12/28/29	12	4	135	72	32.5	96	70	1,010	1,037	— 2	
	4/ 2/30	12	8	137.5	73	34	96	76	1,167	1,065	+ 9	
	11/ 5/30	13	3	140	76	38	96	92	1,440	1,155	+24	Functional murmur; no menses; nervous; tachycardia
	2/16/31	13	6	142	76	39.5	97	112	1,430	1,155	+24	
24 (D. B.)	7/13/29	13	..	152	77	31	88	90	1,392	1,185	+18	Menses at 13 years, 1 month
	1/ 3/30	13	10	155	79	35	90	70	1,228	1,248	— 2	
	7/16/30	14	..	155	79	36	90	72	1,270	1,248	+ 2	
25 (W. McL.)	2/14/28	10	1	130	70	27	93	72	1,000	980	+ 2	
	2/15/29	11	1	136	74	32	93	76	1,140	1,095	+ 4	
	1/ 8/30	12	..	142	76	37	95	80	1,300	1,155	+13	No menses
26 (S. S.)	5/12/28	11	2	125	67	31	99	80	930	897	+ 4	
	3/13/29	12	..	134	70	32	98	78	988	980	+ 1	
	12/ 4/29	12	9	135	73	36	98	78	1,132	1,065	+ 6	
	3/ 8/30	13	..	138	74	40	100	88	1,298	1,095	+19	Menses at 13 years, 3 months
	11/ 1/30	13	8	141	76	43	100	74	1,200	1,155	+ 4	
27 (M. S.)	2/21/28*	12	..	...	..	....	...	..	.....	.....	+21	Record received from another clinic with diagnosis of psychoneurosis
	12/ 1/28*	12	10	...	..	....	...	..	.....	.....	+19	
	5/16/29	13	3	150	78	44.6	101	140	1,632	1,217	+34	Nervous; tremor; tachycardia; goiter
	9/28/29	13	7	152	78	44	98	100	1,368	1,217	+12	Menses at 13 years, 6 months
	1/25/30	13	11	153	80	45.6	97	100	1,488	1,280	+16	
	12/ 6/30	14	10	157	82	49.5	97	88	1,468	1,345	+ 9	
	3/16/31	15	1	157	82	49	97	80	1,398	1,345	+ 4	Much improved
28 (M. H.)	1/22/29	11	2	137	74	30	91	78	1,032	1,095	— 6	
	1/23/30	12	2	141	76	32.2	91	76	1,104	1,155	— 5	
	1/29/31	13	2	148	80	39.5	92	88	1,396	1,280	+10	Menses at 13 years, 2 months

* No measurements recorded.

Boys

29 (H. M.)	7/18/28	12	6	138	73	32	94	62	1,110	1,065	+ 5	
	7/21/29	13	6	145	76	35.8	94	92	1,368	1,155	+19	
	1/29/30	14	..	146	77	35.2	92	74	1,224	1,185	+ 4	Signs of puberty present
	5/29/30	14	4	148	79	38	92	72	1,320	1,248	+ 6	
	1/31/31	15	..	152	80	39.5	92	70	1,309	1,280	+ 3	
30 (S. A.)	6/29/28	13	9	165	86	69	103	80	1,608	1,479	+ 9	
	4/ 5/29	14	7	168	87	65.2	100	100	1,848	1,513	+22	
	6/22/29	14	9	170	87	63	99	78	1,560	1,513	+ 3	
	3/ 1/30	15	8	171	89	67.4	99	72	1,592	1,584	+ 1	Signs of puberty present
	1/31/31	16	6	174	90	67.5	98	72	1,641	1,612	+ 2	
31 (A. L.)	7/ 5/27	13	1	158	82	41	91	68	1,280	1,345	— 5	Simple goiter
	7/ 9/28	14	1	167	87	50	92	86	1,670	1,513	+14	
	3/23/29	14	9	170	89	56	93	80	1,656	1,584	+ 5	
	11/23/29	15	6	171	90	57	93	76	1,629	1,612	+ 1	Signs of puberty present
	6/29/30	16	..	172	90	55	92	72	1,634	1,612	+ 1	
32 (M. M.)	10/12/27	11	3	125	70	29	95	74	1,027	980	+ 5	
	5/26/29	12	10	131	73	32	94	78	1,108	1,065	+ 4	
	11/17/29	13	4	133	73	33	95	78	1,140	1,065	+ 7	
	4/26/30	13	9	139	74	39	95	88	1,296	1,095	+19	
	7/26/30	14	..	141	75	44	96	78	1,185	1,125	+ 6	
33 (G. H.)	3/17/28	12	6	133	72	34	97	70	1,056	1,037	+ 2	
	6/26/29	13	9	135	74	36	97	70	1,032	1,095	— 6	
	9/ 8/29	14	..	141	74	36.5	97	80	1,250	1,095	+14	
	9/16/30	15	..	149	78	41	97	78	1,252	1,216	+ 3	Signs of puberty present
	3/ 7/31	15	6	151	80	45	97	78	1,300	1,280	+ 1	
34 (A. H.)	3/23/29	11	6	135	76	50	105	74	1,146	1,155	— 1	
	6/12/30	12	7	143	79	49	101	76	1,200	1,248	— 4	
	12/27/30	13	1	145	80	50	100	88	1,435	1,280	+12	Functional murmur developed
	3/ 7/31	13	4	147	81	52	100	90	1,536	1,312	+17	
35 (H. C.)	9/23/29	12	6	119	64	25	99	80	902	819	+10	
	9/30/30	13	6	129	67	28	98	90	1,044	897	+17	
	2/28/31	14	..	130	69	29	96	88	1,050	952	+13	
36 (M. E.)	3/ 5/30	12	9	150	79	55	104	70	1,268	1,248	+ 2	
	2/10/31	13	8	155	81	54	101	88	1,558	1,312	+18	
37 (J. L.)	11/14/28	13	7	132	71	31.5	95	66	1,104	1,008	+ 9	
	3/ 2/29	13	11	136	71	31	94	88	1,232	1,008	+22	
	4/15/30	15	..	144	75	34	95	74	1,165	1,125	+ 4	Signs of puberty present
38 (I. D.)	5/ 3/30	13	6	148	77	42	97	90	1,392	1,185	+17	Simple goiter
	3/14/31	14	4	158	82	49	97	76	1,296	1,344	— 4	Signs of puberty present

Göttche [10] found a marked increase in basal metabolism at the beginning of puberty, with a subsequent fall. Bedale [11] found a similar but earlier rise in the metabolism of English girls. Brody and Ragsdale [12] believed that "the age of maximum of the adolescent cycle" comes earlier in England than in other European countries, which may explain the earlier rise in the metabolism of English girls found by Bedale. MacLeod [13] reported an increased metabolism in puberty in a group of American girls. Petenyi and Lax [14] described an increased metabolism at this age period. Janet,[15] in France, corroborated a prepuberty increase in the basal metabolism of French girls. We found an increased basal metabolism in early puberty in a group of obese girls, and again in a group of undernourished girls, both previously reported.[16] Dr. Topper [17] found an increase in the basal metabolism of a group of diabetic girls at the age of from 15 to 16 years, which was coincident with the onset of their menstruation, the catamenia evidently occurring later in diabetic girls than in normal girls (chart 2).

That there should be a rise in the basal metabolism at the time just prior to puberty is not surprising. This is a period when many physical and physiologic changes are taking place, the onset of menstruation itself being a relatively late symptom of the revolution occurring during pubescence. This is the period of greatest growth. In many cases the increase in height for the year just preceding the onset of menstruation was almost twice as great as the increases in height for a similar period after this phenomenon (table, cases 1, 2, 3, 4 ,5, 6, 7, 12, 13, 18 and 26). The increased growth is associated with changes in body form. Girls have a tendency to lay on some fat at this time, especially around the breasts and hips. We noted an increased pelidisi in most of the girls studied (table, column 7). Disturbances of the vasomotor system are common at this period; girls have an increased tendency to blush. In one case (M. K., case 13) the child was made uncomfortable by hot flushes similar to the phenomenon usually associated

10. Gottche, O.: Monatschr. f. Kinderh. **32**:22, 1926.

11. Bedale, E. M.: Proc. Roy. Soc. London, s. B., **94**:368, 1923.

12. Brody, S., and Ragsdale, A. G.: J. Gen. Physiol. **5**:205, 1922.

13. MacLeod, G.: Studies of the Normal Basal Energy Requirements, Inaug. Dissert., Columbia University, 1924.

14. Petenyi, G., and Lax H.: Monatschr. f. Kinderh. **36**:381, 1928.

15. Janet: J. méd. franç. **12**:254 (June) 1923.

16. Topper, A., and Mulier, H.: Basal Metabolism in Children of Abnormal Body Weight: In Underweight Children, Am. J. Dis. Child. **38**:299 (Aug.) 1929. Basal Metabolism of Children of Abnormal Body Weight: Basal Metabolism of Overweight Children, J. A. M. A. **92**:1903 (June 8) 1929.

17. Topper, A.: Basal Metabolism in Diabetic Children, Am. J. Dis. Child. **42**:760 (Oct.) 1931.

with the menopause. This was so strange as to excite independent comment on the part of both of us. There is an awakening of the sexual life at this time. All these significant changes are associated with a greater activity of the endocrine glands. Perhaps at this time, as Biedl [18] suggested, the thyroid gland "if not the conductor, is at least the first violin of the incretory concert," and this may account for the increased basal metabolism found at this time.

Janet believed that there may be a physiologic hyperthyroidism at the period just before puberty. Talbot [19] stated that there are a number of children with enlargement of the thyroid gland, and that these children show evidence of overactivity of the gland at this period. In the present series, seven girls and two boys had an enlarged thyroid gland. These children all had a normal basal metabolism until prepubescence, when the basal metabolic rate rose, and then fell to normal after puberty was well established. But the other children, without enlargement of the thyroid gland, showed a similar increase in their metabolism at this period, which leads us to believe that an increase in basal metabolism is one of the many physiologic manifestations of pubescence.

In some children it becomes important to differentiate the puberty reaction from a serious condition such as organic heart disease, or more especially exophthalmic goiter. Presenting, as these cases may, some of the cardinal symptoms of exophthalmic goiter, such as tremor, nervousness, a palpable thyroid gland, an increased basal metabolic rate (in case 27 it was as high as plus 34 per cent), vasomotor instability and tachycardia, the condition may be mistaken for the more serious syndrome and the gland subjected to destructive treatment. In evaluating high metabolic figures, therefore, at this period, the clinical manifestations of pubescence have to be considered. A high basal metabolic rate is quite physiologic if the child presents other clinical manifestations of pubescence. At this period overactivity of the thyroid gland is temporary and the prognosis is excellent.

SUMMARY AND CONCLUSIONS

The basal metabolism of twenty-eight girls and ten boys from 10 to 16 years of age was studied at intervals of six months to a year over a period of from one to four years.

It was found that there was an increase in the basal metabolic rate in the prepubescent period, reaching its maximum around the time when catamenia was established in girls, and sexual maturity in boys,

18. Biedl, quoted by Herrman, Charles: Pathogenesis of Sporadic Cretinism, Arch. Pediat. **44**:140 (March) 1927.

19. Talbot, F. B.: Monatschr. f. Kinderh. **27**:465, 1924.

with a subsequent decline afterward. There was no uniformity in the height of the increased metabolism, or in the duration of the increase.

Some of these children had no other symptoms of an overacting thyroid gland. Others presented such symptoms as an enlarged thyroid gland, tremor, nervousness, vasomotor instability, cardiac murmur and tachycardia—all of which symptoms disappeared as the basal metabolic rate returned to the previous normal level, when puberty was well established.

We believe that an increased basal metabolism is physiologic during pubescence. This increase coincides with the physiologic age rather than with the chronological age, and occurs earlier in girls than in boys, coincident with their earlier pubescence. As there seems to be an individual variation in the height and duration of the increased metabolism, it makes the adoption of normal standards difficult for this important age period.

The increased basal metabolism may be associated with symptoms simulating organic heart disease, or more especially exophthalmic goiter. Therefore, in evaluating high metabolic figures at this period, the clinical manifestations of pubescence have to be considered. Exophthalmic goiter is rare before puberty, and should not be confused with the physiologic overactivity of the thyroid gland in pubescence, which is temporary and the prognosis of which is excellent.

ANEMIA OF THE NEW-BORN *

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Anemia of the new-born child is a definite, although rare, clinical entity, a few case reports of which have appeared in the literature since 1919 (Ecklin,[1] Donnally,[2] Susstrunk,[3] Sanford,[4] Schleussing,[5] Foote,[6] Bonar,[7] Canino,[8] Foote,[9] Ehrmann,[10] Greenthal,[11] Happ,[12] Gelston and Sappington,[13] and Blackfan et al.[14]).

The following clinical manifestations have been noted in all accepted cases (table 2): The infants are born of healthy parents, in normal spontaneous labor, and from their history has been excluded all evidence of birth injury, hemorrhage, hemorrhagic disease, infection or prenatal poisoning. Within the first two weeks of life these infants, while thriving and behaving in every way as normal new-born infants, become extremely pale. This pallor is a sheetlike whiteness; in several cases it

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1. Ecklin, T.: Ein Fall von Anämie bei einem Neugeborenen, Monatschr, f. Kinderh. **15**:425, 1919.

2. Donnally, H. H.: Anemia in the New-Born, Am. J. Dis. Child. **27**:369 (April) 1924.

3. Susstrunk, G.: Schwerste Anämie bei einem Neugeborenen, Ztschr. f. Kinderh. **38**:587 (Aug.) 1924.

4. Sanford, H. N.: Anemia in the New-Born Infant, Am. J. Dis. Child. **30**:19 (July) 1925.

5. Schleussing, H.: Beitrag zur den sogenannten Anämien der Neugeborenen, Verhandl. d. deutsch. path. Gesellsch. **21**:371, 1926.

6. Foote, John: Diseases of the New-Born, Philadelphia, J. B. Lippincott Company, 1926, p. 59.

7. Bonar, B. E.: Anemia in the New-Born, Am. J. Dis. Child. **33**:226 (Feb.) 1927.

8. Canino, R.: Un caso di anemia in un neonato, Pediatria **35**:1299 (Dec.) 1927.

9. Foote, John: Anemia primitiva en los recién nacidos, Arch. am. de med. **4**: 39 (April) 1928.

10. Ehrmann, E. W.: Anemia of the New-Born Infant, Am. J. Dis. Child. **37**: 138 (Jan.) 1929.

11. Greenthal, R. M.: Anemia of the New-Born, Am. J. M. Sc. **179**:66 (Jan.) 1930

12. Happ, W. M.: Idiopathic Anemia of the New-Born Infant, Arch. Pediat. **47**:171 (March) 1930.

13. Gelston, C. F., and Sappington, E. E.: Primary Anemia in the New-Born, Am. J. Dis. Child. **39**: 807 (April) 1930.

14. Blackfan, K. D.: Oxford Monographs on Diagnosis and Treatment, New York, Oxford University Press, 1930, vol. 9, p. 546.

was reported by the nurse, attendant or mother that the infant was as pale as the white bed sheets. The infants nurse well, are afebrile, have normal periods of sleep and wakefulness, cry lustily and vigorously, and, aside from the marked and startling pallor, show no signs of ill-being. Recovery has been observed, both without and with treatment, and infants who have been followed for several years have shown no residual effects.

Of the various titles under which reports of this condition have appeared, "Anemia of the New-Born" is the most appropriate, until the exact etiology of the condition has been proved.

Before the first clinical observation was reported by Ecklin,[1] in 1919, the possibility of the occurrence of this condition was speculated on. Finkelstein,[15] in 1911, mentioned a type of anemia in new-born children marked by a severe reduction of hemoglobin and corpuscular elements of the blood, and Lichtenstein,[16] in 1917, stated that he could not altogether exclude the possibility that an unequivocal case of congenital anemia might be found.

I wish to report in detail a typical case of anemia of the new-born in which the hematologic study incidentally revealed abnormal mononuclear cells in the circulating blood which had ingested erythrocytes—mononuclear erythrophagocytosis.

REPORT OF A CASE

History.—The mother, white, aged 34, had been perfectly well during her seventh pregnancy. Her blood pressure was 110 systolic and 70 diastolic, and her weight was 137 pounds (62.1 Kg.). All previous children were living and well. There had been no miscarriages and no stillbirths. The father was well. The Wassermann and Kahn reactions of both parents were negative. There was no history of tuberculosis in the family.

Labor commenced at 2 a. m., on Dec. 11, 1926. The duration of the first stage was five hours, of the second stage, twenty-seven minutes and of the third stage, ten minutes. The membranes ruptured at 7:15 a. m., and birth occurred at 7:27 a. m. Delivery was normal and spontaneous; no forceps was used, and no anesthetic was necessary. The infant cried immediately, and the cord was tied, with no bleeding of the baby. The mother went home on the tenth day, discharged as perfectly well.

The infant's color was pink. The birth weight was 2,631 Gm. (5 pounds, 8 ounces), and the temperature was 97 F. She lost 120 Gm. after birth, and began to gain weight on the third day. She was fed at the breast every four hours, and received from 1 to 2½ ounces of breast milk plus some complementary formula. The baby had no fever at any time, her temperature ranging from 98.2 and

15. Finkelstein, H.: Ueber die Anämien des früheren Kindesalters, Berl. klin. Wchnschr. **48**:1829, 1911.

16. Lichtenstein, A., abstr. by Denzer, B. S.: Hematological Studies of Premature Babies During Infancy with Particular Reference to Anemic Conditions, Arch. Pediat. **43**:741 (Nov.) 1926.

TABLE 1.—*Blood Counts and Differential Blood Picture in Case Presented*

Age	Smear	Red Blood Cells	Hemoglobin (Sahli), per Cent	White Blood Cells	Myelocytes		Polymorphonuclears	Myeloblasts	Eosinophils	Basophils	Small Lymphocytes	Large Lymphocytes	Monocytes	Monocytes with Phagocytosed Erythrocytes	Total per Cent of White Blood Cells	Abnormal R.B.C. per 100 W.B.C.	
					Promyelocytes	Neutrophilic Myelocytes										Normoblasts	Basophilic Erythroblasts
9 days	Wright, 100 cells	1,270,000	24	35,000	4	9	34	3	2	1	28	6	9	4	100	22	4
11 days	Wright, 100 cells	1,320,000	25	30,000	4	11	38	2	1	2	24	7	6	5	100	32	5
12 days	Wright, 100 cells	1,480,000	28	21,000	5	6	32	2	1	1	32	10	8	3	100	25	2
15 days	Major Grunwald, Giemsa, 250 cells	1,820,000	30	18,500	0	4	49	1	3	2	30	3	6	2	100	11	0
20 days	Wright, 100 cells	2,260,000	35	14,300	0	0	51	0	1	3	36	8	1	0	100	2	0
25 days	Wright, 100 cells	2,650,000	38	16,400	0	0	43	0	2	2	39	12	2	0	100	0	0
1 mo.	Wright, 100 cells	2,540,000	45	10,250	0	0	31	0	2	1	52	11	3	0	100	0	0
6 wks.	Wright, 100 cells	3,200,000	55	11,500	0	0	36	0	2	1	45	14	2	0	100	0	0
2 mos.	Wright, 100 cells	4,050,000	58	9,850	0	0	41	0	3	1	38	13	4	0	100	0	0
4 mos.	Wright, 100 cells	3,200,000	55	10,300	0	..	39	..	1	1	48	8	3	0	100	0	0
8 mos.	Wright, 100 cells	3,830,000	68	9,950	..	0	42	0	1	2	50	3	2	0	100	0	0
13 mos.	Wright, 100 cells	4,250,000	75	8,700	0	0	46	0	2	1	42	5	4	0	100	0	0

98.8 F. The urine and stools were normal, and no jaundice was noted. The pallor was observed by the nurses on the eighth day. On the ninth day, the child seemed as white as the sheet on which it lay. The cord fell off on the fifth day; there were no hemorrhages from the umbilicus, no petechiae and no melena. The infant was transferred to the pediatric service on the ninth day.

Examination.—Physical examination at the age of 9 days revealed a well formed girl, weighing 5 pounds and 6 ounces (2,438 Gm.), with marked, intense pallor and no jaundice, petechiae or ecchymoses. The skin was smooth and moist, with normal turgor. The child cried when stimulated; she was in no apparent pain or distress. The baby took its feedings and water eagerly when offered.

There was no general glandular enlargement; the mucous membranes of the conjunctivae and buccal cavities were pale. The ear lobes were white, and the finger-nails and toe-nails showed marked pallor. There was no bulging of the fontanel; the eyes reacted normally to light and in accommodation, and there was no nystagmus. The throat was clear. The lungs were resonant throughout, and the breath sounds vesicular; the heart tones were clear, and there were no murmurs. The abdomen was scaphoid; there was no distention, and no masses were palpated. The liver was palpable one fingerbreadth below the costal margin, and the lower pole of the spleen was just felt. The extremities, genitalia and reflexes were normal. Examination of the fundi and eyegrounds showed normal disks, retina, pigment and blood vessels.

Morphologic examination of the blood showed an unusual picture; the chief findings are summarized in table 1. Most prominent among these were a marked decrease in the number of erythrocytes, a low hemoglobin content and moderate leukocytosis, with a normal differential count, except for a slight high monocyte value and the presence of phagocytosed erythrocytes in some of the latter cells. In addition, the number of basophil and orthochromatic erythroblasts (normoblasts) was increased.

The red blood cells showed moderate anisocytosis and slight poikilocytosis on all blood smears taken up to 1 month of age. The erythrocytes frequently showed diffuse and punctate basophilia. Vital stains, made on the twelfth day of life with neutral red and janus green, showed normally motile leukocytes and several mononuclears, with ingested erythrocytes which were seen to be motile.

In short, the blood picture was that of a severe secondary anemia with marked evidence of regeneration, as shown by the erythrocyte precursors circulating in the blood. The most unusual part of the picture, however, was the erythrophagocytosis by the circulating monocytes.

Coagulation time on the eleventh day was two minutes and thirty seconds; the platelet count, 480,000, and the bleeding time, four minutes. The fragility test showed hemolysis beginning at 0.42 per cent and complete at 0.36 per cent (normal values).

All urinary examinations gave normal results; the Wassermann and Kahn reactions were both negative when the infant was 6 weeks of age.

Course.—The child was placed on breast milk with a supplementary cow's milk formula. It took its feedings and water eagerly, and gained gradually and steadily in weight. The stools were of normal consistency and number.

No medication whatever was attempted; no iron salts were given, and no blood was tranfused, either intramuscularly or intravenously. At 4 weeks of age, orange juice was started, and at 6 weeks, cod liver oil. The infant was discharged at the age of 2 months.

Chickenpox developed at 3½ months of age, and the skin still showed a few healed scars when the infant was examined at 4 months of age. The skin and

mucous membranes showed only slight pallor at this age, and the child was gaining well. The fontanel was closing, and no craniotabes or enlargement of the costochondral junctions were noted; the spleen was not felt.

At 8 months of age, the infant weighed 16 pounds, 14 ounces (7.6 Kg.). The fontanel was closing; there were no rachitic manifestations; the child had cut the two lower incisor teeth, and the spleen was not felt.

At 13 months of age, the fontanel had closed; the baby stood and attempted to walk. Its development was physically and mentally normal in every way.

TERMINOLOGY

Anemia of the new-born has also been termed, by various authors, idiopathic, primary or congenital anemia. Since the explanation of the exact mechanism of the cause of this anemia is as yet unknown, the term idiopathic is objectionable, because it conveys no definite meaning. These anemias are of a secondary type and should not be confused with primary pernicious anemia. The congenital nature of the disease has not been proved. Hence to speak of this condition, or even of the well known late type of anemia commonly developing in premature infants, as of congenital origin is evidence of a misconception of those conditions, as will be pointed out.

ANEMIA OF NEW-BORN INFANTS KNOWN TO BE DUE TO A SPECIFIC CAUSE

There are certain agents that are known to produce anemia in the new-born. Some of them are here enumerated; obviously they do not apply to the type of disease that is designated as anemia of the new-born of unknown cause.

The anemia of the premature infant develops gradually from the fifth week on, and sufficient investigation of this anemia has been carried out to differentiate it clearly as a definite type.[14]

Actual hemorrhage, such as bleeding from the cord, hemorrhage from circumcision in hemophilia, asphyxia or traumatic injuries to the internal viscera during birth, should be ruled out. Likewise, meningeal or cerebral hemorrhage can be distinguished by the accompanying cerebral signs, and hemorrhagic disease of the new-born is associated with melena, epistaxis, hematuria and bleeding from other organs. Rare diseases of the new-born, such as congenital ascites, familial icterus gravis, Winckel's disease, Buhl's disease, severe sepsis and all pyogenic infections, may cause severe anemia.[7]

Congenital syphilis [17] must always be considered as a possible cause of anemia in the new-born, as well as congenital malaria and, most rarely, congenital tuberculosis.

17. Barbour, P. F.: Anemia of the New-Born, South. M. J. **24**: 107 (Feb.) 1931.

Inorganic poisons or poisoning due to lead and organic compounds, such as benzene and acetanilid, may affect the fetus through the mother, and roentgen rays and radium may produce anemia in the mother and fetus.[2]

In contradistinction to these poisons, it has been definitely shown that there is a distinct and positive separation between maternal and fetal blood formation. The anemia of the mother is not carried over to the new-born child,[18] even in such definite maternal conditions as severe pernicious anemia, secondary anemia or leukemia.

ANALYSIS OF CASES REPORTED IN THE LITERATURE

In an analysis of all of the reported cases of anemia of the new-born (table 2), the family history and the health of the parents and of other previously born children were entirely normal, with the exception of the cases reported by Ecklin,[1] Susstrunk,[8] Greenthal [11] and Happ.[12] In Ecklin's case, the father was reported to have had cardiac disease, and the mother had an attack of severe grip and bronchitis during pregnancy. The child of the preceeding pregnancy had died of icterus gravis at 17 days of age. In Susstrunk's report, while both parents were well, there had been seven stillbirths in previous pregnancies. Both Greenthal and Happ reported serious illness in the mother. The former reported a primipara with hypertensive and eclamptic symptoms, and the latter reported a mother with tuberculous pleurisy.

The birth histories were normal in all cases, except those reported by Foote in 1928 and 1929, Ehrmann,[10] Greenthal,[11] and Happ.[12] In Foote's first reported case, the labor was slow, with the aid of forceps, while in his second case, the infant was a premature twin. Ehrmann reported a breech delivery after short labor. Greenthal's case showed positive evidence of intracranial hemorrhage after high forceps delivery, with bulging fontanel and bloody spinal fluid. In Happ's case, the baby was born asphyxiated with the cord around the neck. Prolonged artificial respiration and epinephrine injected into the heart finally aroused the infant. This child was too weak to nurse.

The birth weights averaged from 2,631 Gm. (5½ pounds) to 3,500 Gm. (7 pounds, 9 ounces), with the exception of Foote's premature twin, who weighed 1,326 Gm. Severe icterus was present only in Susstrunk's patient, and slight icterus, when reported, occurred in four cases. Icterus was noted as entirely absent in five cases. The spleen was definitely enlarged in only one case, slightly palpable in seven cases and not felt in five cases. The anemia was earliest noted at 1 day of age.[4] The average age for the appearance of the anemia was between

18. Baar-Stransky: Die klinische Hämatologie des Kindesalters, Vienna, Franz Deuticke, 1928, pp. 16 and 26.

7 and 8 days. The number of erythrocytes ranged between 650,000 and 2,500,000. The hemoglobin ranged between 15 per cent and 48 per cent. The white blood count varied from 11,000 to 40,000. There were moderate anisocytosis and slight poikilocytosis in all cases. There was a moderate increase in normoblasts above the average, while diffuse and punctate basophilia was slight.

The differential counts were within normal limits for the new-born as regards both the polymorphonuclear and the lymphocytic cells. A few myelocytes and myeloblasts were noted. The case reported here is the only one in which mononuclear erythrophagocytosis was observed. The platelet count ranged within normal limits; the coagulation and bleeding times were not prolonged. The fragility test was twice reported as normal and once as prolonged. The age at which the anemia disappeared ranged from 2 to 6 months, and all the infants who survived developed normally. No treatment whatever was employed in five cases of the infants who survived, and in five of the undisputed cases, transfusion of blood was performed from one to three times. Two infants have been reported entirely normal at 3½ years of age. Two infants died at the fourth and tenth days of life.

Two autopsies were reported, by Susstrunk [3] and by Schleussing.[5] In Susstrunk's case, the gross pathologic process showed grave icterus and anemia, hemosiderosis of the liver and spleen, hematoma of the cardiac valves and hemorrhages into the pelvis of the kidney and the urinary bladder. Microscopically, the liver showed a sparsity of blood-forming islands.

The autopsy in Schleussing's case showed no gross abnormalities. Microscopically, blood-forming islands were numerous in the liver, spleen and bone marrow, and in the connective tissue of the blood vessels of the lung, pancreas, kidney, suprarenals and lymph nodes.

Of the reported cases that I have analyzed in detail, I would exclude on etiologic grounds the cases of Susstrunk, Greenthal and Happ from being true examples of anemia of the new-born of unknown cause. Greenthal's case showed positive evidence of cerebral hemorrhage after high forceps delivery, and Happ's case, a tuberculous mother and an extreme type of asphyxia neonatorum. Susstrunk's case showed grave icterus at autopsy. Foote's case of the premature twin is doubtful, as the prematurity might have accounted for the anemia.

ETIOLOGY

While various theories have been advanced to explain the anemia, none has yet been offered that will convincingly explain the fundamental conditions of its occurrence.

TABLE 2.—*Summary of Cases of Anemia of the N... Taken fr...*

	1	2	3*†	4	5	6	7	8
Author	Ecklin, T.	Donnally, H. H.	Susstrunk, G.	Sanford, H.E.	Schleussing, H.	Foote, John	Bonar, B. ...	...o, R.
Date	1919	April, 1924	August, 1924	July, 1925	1926	1926	1927	
Family history	Father, heart disease; mother, grip during pregnancy; 1 sibling died, aged 17 days of familial icterus gravis	Parents well; no miscarriages; 1 child living and well	Parents well; 14 siblings, 7 stillbirths, 3 siblings died in infancy	Parents well; 1 sibling living and well	Parents well	.....	Parents w... 4 siblings l... ing and w... 1 died, age... days, of h... orrhage; 1... tion, at 6 w...	...nts well
Wassermann reaction of the parents	Mother, negative	Both parents, negative	Mother, negative	Mother, negative	Father and mother, negative	.....	Negative	.....
Birth history	Spontaneous	Normal and spontaneous	Spontaneous	Spontaneous	Spontaneous	Slow labor, by forceps	Spontaneo...	...nal
Injuries, etc.	Normal	Slight convulsions on 2d and 3d days	Normal	Normal	Normal	.....	Normal	...
Birth weight	2,870 Gm. (6 lb., 5 oz.)	3,516 Gm. (7 lb., 10 oz.)	3,200 Gm. (6 lb., 15 oz.)	3,000 Gm. (6 lb., 8 oz.)	.....	.....	3,175 Gm. (7 lb.)	... Gm. ..., 1 oz.)
Jaundice	First to sixteenth day	Absent	Severe icterus, third day	Moderate, from second to sixth days	Second to third day	.....	Absent	...t to ...d day
Spleen	3 cm. below costal margin	Barely palpable	Palpable	Palpable	Slightly palpable	.....	Not palpab...	...palpable
Blood examination, stain; day of life	May Grenwald; twelfth day	Twelfth day	Seventh day	First day	Third day	Seventh day	Thirteenth day	...lfth day
Red blood cells	2,500,000	918,000	1,150,000	2,500,000	2,060,000	960,000	1,200,000	...,000
Hemoglobin	32%, Sahli	20%	26%, Sahli	48%, Dare	45%, Antenweth	20%	31%, Dare	...
White blood cells	40,000	29,200	10,600	68,400	2,600	.....	18,000	...0
Color index	0.64	1	1.1	0.96	1.1	.....	1.3	...
Red blood cells:								
Anisocytes	+++	+	+	.....	+	.....	+	...
Poikilocytes	+	±	+	+	±	.....	+	...
Color	Pale	Normal	.....	.....	.....	.....	.....	.....
Normoblasts	17/100 W.B.C.¶	10/300 W.B.C.	1/100 W.B.C.	15/200 W.B.C.	190/200 W.B.C.	.....	Occasional	...0 W.B.C.
Basophilic	.....	.....	.....	.....	.....	.....	.....	...
Basophilia:								
Diffuse	++	++	.....	.....	.....	.....	.....	...
Punctate	+	+	.....	.....	.....	.....	.....	.....
Reticulocytes	.....	4.6% (4 weeks)	.....	.....	.....	.....	.....	.....

ia of the l *Taken from the Literature in Chronological Order*

7	8	9*‡	10	11*§	12*#	13	14	15
Bonar, B.	no, R.	Foote, John	Ehrmann, E. W.	Greenthal, R. M.	Happ, W. M.	Gelston, C. F., and Sapping-ton, E. E.	Blackfan, K. D., et al.	Abt, A. F.,
1927		April, 1928	January, 1929	January, 1930	March, 1930	April, 1930	1930	April, 1931
Parents w 4 siblings l ing and wel 1 died, age days, of be orrhage; 1 tion, at 6 w	nts well		Parents well; 1 sibling liv-ing and well	Mother; hyper-tension, tox-emia, primipara	Mother, tuber-culosis, pleurisy; baby born with cord around neck; asphyxiated	Mother well 1 sibling liv-ing and well	Parents well; 2 siblings liv-ing and well	Parents well; 6 siblings liv-ing and well
Negative	...	.....	.....	.....	Mother, negative	Mother, negative	No test made	Mother and father, negative
Spontaneo	nal	Premature twin	Breech, short labor of 4 hours	High forceps, instrumental	Low forceps	Spontaneous	Spontaneous	Spontaneous
Normal	....	.....	.....	Bloody spinal fluid; bulging fontanelle	Prolonged arti-ficial respiration; epinephrine injected into heart; too weak to nurse	Normal	Normal	Normal
175 Gm. 7 lb.)	Gm. ., 1 oz.)	1,326 Gm.	3,500 Gm. (7 lb., 9½ oz.)	2,690 Gm. (5 lb., 9½ oz.)	3,100 Gm. (6 lb., 11 oz.)	3,200 Gm. (7 lb., 7 oz.)	3,500 Gm. (7 lb., 9 oz.)	2,631 Gm. (5 lb., 8 oz.)
bsent	t to d day	.....	Absent	.....	Absent	.....	.....	Absent
ot palpab	palpable	.....	Not palpable	Not palpable	Not palpable	Slightly palpable	Slightly palpable	Slightly palpable
irteenth y	fth day	Second month	Fifth day	Second day	Fifteenth day	Seventh day	Seventeenth day	Ninth day
00,000	,000	2,800,000	1,228,000	1,178,000	1,088,000	2,300,000	650,000	1,270,000
%, Dare		35%	28%, Dare	48%	40%, Sahli	42%	15%, Newman	24%, Sahli
00	0	5,200	20,550	17,000	11,200	12,400	16,150	35,000
		.....	1.2	1.3	.....	.....	1.15	0.96
		.....	+	+	+	+	+	+++
		.....	+	.....	+	+	+	+
....	....	.....	.....	.....	.....	.....	.....	Slight pallor
asional	0 W.B.C.	++	7/200 W.B.C.	Few	Few	1/100 W.B.C.	Few	22/100 W.B.C.
....		+	.....	.....	.....	.....	.....	4/100 W.B.C.
....		.....	+	.....	+	+	+	+
....	....	.....	+	.....	.....	.....	.....	.....
....	....	.....	.....	.....	.....	.....	2%	.....

TABLE 2.—*Summary of Cases of Anemia of the New-B*

	1	2	3	4	5	6	7
White blood cells:							
1. Polymorphonuclears	39.6%	51.3%	33%	60%	43%	.....	54%
2. Myelocytes:							
3. Promyelocytes...	4.0%	.....	.....	.....	.....	Few	.....
4. Neutrophilic myelocytes	3.3%	.....	.....	.....	2%	Few	.....
5. Myeloblasts.....	None	None	None	None	None	.....	None
6. Eosinophilic polymorphonuclears	.....	0.7%	0.8%	3%	.....	.....	.....
7. Basophilic polymorphonuclears	.....	0	0.2%	.....	.....	.....	.....
8. Small lymphocytes 9. Large lymphocytes	57.8%	42%	60%	35%	53%	.....	43% 3%
10. Large monocytes	2.6%	2.7%	5.6%	2%	2%	.....	.....
11. Large monocytes with phagocytosis	None	None	None	None	None	.....	None
Platelets.....	.....	Increased	Numerous	285,000	.....	.....	.....
Coagulation Time	.....	.....	.....	.....	4 min.	.....	.....
Bleeding time					5 min.		
Fragility test.....	.....	.....	.....	.....	.....	.....	.....
Blood picture return to normal	Approximately 7 mo.	Within 6 mo.	.....	Within 1 mo.	.....	Within 1 year	At 1 year
Medication and treatment	None	1. Two transfusions 2. Fowler's solution 3. Beef juice and spinach	None	None	None	Two transfusions	None
Outcome.....	Normal development	Normal development	Died tenth day	Normal development	Died fourth day	.....	Normal development
Pallor noted.....	Eighth day	Eleventh day	Seventh day	First day	First day	Seventh day	Thirteenth da

* Cases that probably do not belong to this group.
† The severe jaundice of the infant points to familial icterus gravis neonatorum.
‡ This was probably a case of early premature anemia.
§ The mother was eclamptic, with hypertension. The child was delivered by forceps with difficulty, and showed definite sig
of birth injury.

n from the Literature in Chronological Order—Continued

7	8	9	10	11	12	13	14	15
4%		.....	36%	76%	30%	56%	52%	34%
.....		.....	.....	.....	.....	.....	.....	4%
.....		.....	.....	.....	.....	.....	.....	9%
one		.....	2%	.....	.....	.....	8%	3%
.....		.....	1%	1%	2%	3%	2%	2%
.....		.....	0	.....	.....	.....	1%	1%
%		.....	30%	18%	52%	41%	32%	28%
		.....	26%					6%
.....		.....	5%	5%	16%	.....	5%	9%
ne		.....	None	None	None	None	None	4%
.....		.....	334,000	260,000	Normal	.....	430,000	480,000
.....	n.	.....	4 min.	.....	.....	6 min.	Normal	2½ min.
			3½ min.			1 min.	2 min.	4 min.
....		.....	0.6%–0.44%	.....	.....	.....	0.44%–0.34%	0.42%–0.36%
t year	nths	4 months	7 months	4 months	4 months	4 months	4 months	2 months
e		Transfusion of citrated blood	Two intraperitoneal transfusions	Direct transfusion	Three transfusions intravenously	Three transfusions intravenously	Three transfusions intravenously	None
nal lopment	nal lopment	Normal development	Normal development	Normal development	Normal development	Normal development	Normal development	Normal development
teenth da	d day	Eighth day	Fifth day	Second day	Fifteenth day	Seventh day	Seventeenth day	Eighth day

finite sig

Tuberculous pleurisy developed in the mother. The infant was deeply axphyxiated by the cord around its neck. It was ed with difficulty, and was too weak to nurse.

In each case this figure represents the number of normoblasts per the number of white blood cells counted.

It has been suggested that toxic elements may increase blood destruction,[1] though there are no signs of such action on other organs, such as jaundice, hematuria, nephritis or cerebral symptoms. The anemia may occur through an essential weakness of the hematopoietic system [16] or, as Foote [19] has suggested, it may be due to an early exhaustion of an insufficient blood depot supply. However, why should this exhaustion occur within the first two weeks of life, when ordinarily it appears only in the full term infant in the second half of the first year of life, and in the premature infant after the first month?

Ehrmann's [9] suggestion that there is increased fragility of the erythrocytes was not substantiated by Blackfan [13] or myself.

Salomonsen [20] has recently pointed out that blood formation and blood destruction in the new-born are part of a series of processes in the adaption of the child to extrafetal life. The fetus, living in a low oxygen tension, is suddenly at birth placed in an environment containing a free supply of oxygen, when the lungs expand. This improvement in oxygenization removes the cause for fetal polycythemia, and the excess red blood corpuscles are removed.

"But the more intimate, exact mechanisms by which such wonderful adaptations can be accomplished are fundamental problems that await further elucidation." [21] Until the exact mechanism of the normal adaptation of the blood-forming and blood-destroying processes in this early period is known, anemia of the new-born cannot adequately be explained.

COMMENT ON MONONUCLEAR ERYTHROPHAGOCYTOSIS

The occurrence of phagocytic mononuclear leukocytes in the circulating blood in the case of anemia of the new-born reported can be described as a rare incidental hematologic finding probably unrelated to the etiology of this condition. In view of the few erythrocyte-containing phagocytes seen in the blood smears, it would be unwise to assume that enough erythrocytes had been ingested by circulating mononuclear cells to account for the degree of anemia. The extent to which erythrophagocytosis may have taken place in the fixed phagocytes of the body in my case is, of course, undetermined. As far as I can ascertain, circulating mononuclear cells with ingested erythrocytes have never been reported in the blood of the new-born human infant.[22]

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19. Foote, John: Anemia of the New-Born, Am. J. Dis. Child. **39**:1302 (June) 1930.

20. Salomonsen, Leif: Physiologic Hematopoiesis and Hemolysin in the New-Born, Norsk mag. f. laegevidensk. **91**:1299 (Dec.) 1930.

21. Editorial: The Blood in the New-Born, J. A. M. A. **96**:197 (Jan. 17) 1931.

22. Lippman, H. A.: A Morphologic and Quantitative Study of the Blood Corpuscles in the New-Born Period, Am. J. Dis. Child. **27**:473 (May) 1924.

In reviewing the literature on mononuclear phagocytosis in circulating human blood, I found that it may occur in a great diversity of diseases, and that it may also be produced experimentally in animals. The only reports of its occurrence in an infant or child that I was able to find were in the cases of malarial infection reported by Connal [23] in native South African children. A detailed report on mononuclear erythrophagocytosis appears in a previous paper.[24]

CONCLUSION

Anemia of the new-born of unknown cause has been chosen as the most appropriate terminology for the condition in a group of reported cases in which new-born infants of healthy parents, born in normal labor and from whose history hemorrhage or loss of blood has been carefully excluded, suddenly become profoundly anemic within the first fourteen days of life. These babies, except for the suddenly developing anemia, have shown no other abnormalities, behaving in every other way as normal new-born infants. They have gradually recovered without demonstrable residual effect, both without and with medication and the transfusion of blood.

The reported cases found in the literature have been analyzed in detail.[25] I have reported an additional case, the blood findings of which differed from those previously reported, in that a rare hematologic finding, mononuclear erythrophagocytosis, was present in the circulating blood. This condition probably has no bearing on the etiology of anemia of the new-born.

The various possible etiologic factors that might produce this anemia have been discussed, but until the exact mechanism of the normal adaption of the blood-forming and blood-destroying processes during the new-born period are more clearly understood, the exact etiologic factor cannot be determined.

104 South Michigan Avenue.

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23. Connal, A.: Auto-Erythrophagocytosis in Protozoal Diseases, J. Path. & Bact. **16**:502, 1912.

24. Abt, A. F.: Mononuclear Erythrophagocytosis in the Blood of a New-Born Infant, Am. J. Dis. Child. **42**:1364 (Dec.) 1931.

25. Since this article was submitted for publication, two additional contributions on anemia of the new-born have appeared in the most recent literature: Stransky, Eugen: Beiträge zur klinischen Hämatologie im Säuglingsalter: X. Mitteilung. Ueber die primäre Anämie der Neugeborenen, Ztschr. f. Kinderh. **51**:239 (June 27) 1931. Pasachoff, H. D., and Wilson Leo: Congenital Anemia of the New-Born, Am. J. Dis. Child. **42**:111 (July) 1931.

A SIMPLE, RATIONAL AND EFFECTIVE TREATMENT OF STUBBORN VAGINAL INFECTIONS IN INFANTS AND IN LITTLE GIRLS*

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There is definite need for a revision of antiquated ideas and some clear, simple instructions in regard to the management of vaginal infection in the immature. I shall limit this discussion to the treatment for this condition [1] and to the cause only in so far as is necessary to a clear understanding of the reasons for a modified technic. Directions and illustrations are purposely simple and fundamental for the reason that I am convinced that many physicians have no clear conception even of the gross anatomy of the infantile female genitalia.

RATIONAL CONCEPT OF ETIOLOGY

The time worn theory that the infantile vaginal canal is carpeted by a thin, weakly resistant mucous membrane is untenable, as proved by repeated gross and microscopic examinations. In the infant and small child, the vaginal canal constitutes an ideal "harbor of infection," whereas in the adult it does not. Obvious characteristics of the immature vagina account for mechanical retention of organisms and for changes in the secretions favorable to their existence. These are: (1) hymenal occlusion (relative) (figs. 1 and 2); (2) the contracted cryptiform accordian-like conformation (fig. 3).

These are factors that operate definitely in immature and virginal persons, are absent in parous adults (figs. 2 and 3) and present in varying degrees in women who have had intercourse but no children. It is enlightening in this regard to note that the occasional primary vaginitis seen in the adult (*Trichomonas* infection excepted) occurs

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* Read before the Portland Society of Obstetricians and Gynecologists, Jan. 29, 1930, and before the Northwest Pediatric Society, Jan. 24, 1931.

1. The so-called "cervico-vaginitis" noted by Hess and recently stressed by Irving Stein, as I have pointed out before, comes under this discussion. In this condition the vaginal portion of the cervix is involved, but not the endocervix. It is amenable to efficient vaginal treatment. Endocervicitis, bartholinitis, urethritis, skenitis and proctitis will not be discussed here.

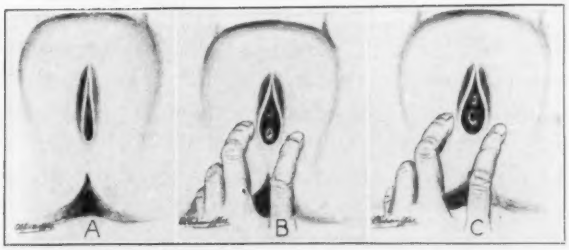

Fig. 1.—*A*, normal habitus. *B*, the index and second finger of the left hand are gently but firmly placed at either side of the fourchette, and gentle pressure is made posteriorly and laterally with each finger. This will open the vulva and expose the hymen. *C*, the child is now instructed to bear down as if having a bowel movement. If this instruction is followed correctly there will be a resultant pouting of the lips of the hymenal opening. An exact knowledge of the location and shape of this opening is essential to a careful and gentle technic.

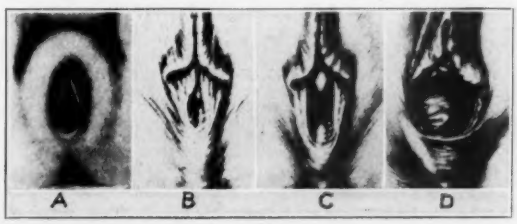

Fig. 2.—Relative occlusion at the vaginal outlet. *A*, infantile habitus; complete occlusion save for hymenal opening 4 mm. in diameter. *B*, the nulliparous introitus of a married woman. There is no actual obstruction; drainage is free. *C* shows the parous introitus with moderate relaxation, and *D*, the parous introitus with considerable relaxation following a second degree tear. The vaginal wall in these cases is flattened, and there is no tendency to occlusion at the outlet. Drainage is free. There are no crypts to serve as harbors for delicate organisms, such as the gonococcus.

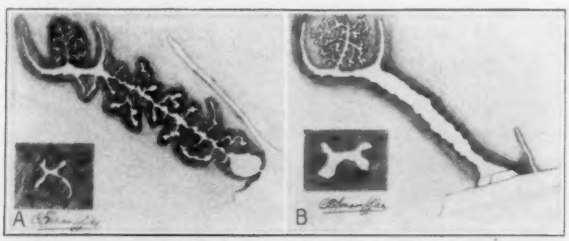

Fig. 3.—Diagrammatic sagittal section of *A*, early infantile vagina, showing a cryptic accordian-like conformation. The walls are held in contact by the natural elasticity and tenacity of the mucous covered surfaces. There are many static crypts or "harbors" not reached by ordinary methods of treatment. The relative hymenal occlusion is well shown. *B*, topography of parous adult vagina. Note the comparative flatness, absence of crypts, i. e., accessibility to medicaments, and hymenal patency (cross-sections are shown in the insets).

almost without exception in unmarried virginal persons. Here the same factors of hymenal occlusion and cryptiform contraction of the vagina are active, though perhaps in a minor degree. One recognizes also a primary vaginitis of senility. Here the factor of obstruction is often present through the agency of contractures and fibrous septums, while the factor of decreased local resistance is an actuality.

TREATMENT

The immature vagina, then, constitutes an actual "harbor of infection." The mature vagina, with exceptions as noted, does not. With these facts clearly in mind, one can approach the matter of treatment intelligently. The indication is for the thorough application of a reliable antiseptic which will be penetrative and effective over a long period. This indication has not been met by the majority of methods now in use, for example:

The vaginal douche consists in squirting into the vagina varying amounts of a very weak antiseptic solution which washes off the tops of the rugae and runs out immediately. It is quite unsatisfactory in the adult and absolutely so in the infant.

Instillations of stronger antiseptics, if they are sufficiently concentrated, may irritate and do not achieve a complete application. With the child in the knee-chest position, a better result may be gained, but it can be shown that little or no additional distention is thus obtained in children. The antiseptic is better retained thus, but the average application includes by no means the entire vaginal surface. The method is superior to douching and will control the mild infections.

Suppositories bearing antiseptics in appropriate concentration are more satisfactory than any form of liquid medication. There is some distention occasioned when the suppository is introduced, and the application is rather more complete and lasting. Suppositories may be highly desirable as an adjunct to office treatment and constitute the best method of home treatment. They do not, however, fulfil the requirements for the most efficient treatment.

Ointments, particularly if compounded in a heavy base, such as wool fat, constitute the best treatment medium. Any reliable antiseptic, thus incorporated, will be relatively efficient. Gelhorn and Stein have for several years advocated the use of 1 per cent mercurochrome-220 incorporated in hydrous wool fat mixed with an equal amount of petrolatum. The mixture is warmed to softness, injected high into the vagina and allowed to flow out around the catheter. The disadvantages of this method are: (1) the ointment is not made to penetrate to all parts

Fig. 4.—Treatment for vaginitis with ointment. *A*, actual result with the use of a soft base of warmed wool fat ointment injected through a catheter. The crypts are not invaded. The application is not universal. *B*, result of injection under moderate pressure of hard base (anhydrous wool fat) ointment by Schauffler's technic; invasion of all crypts—universal application. The penetration is due to pressure, the anhydrous base and the use of antiseptic dye.

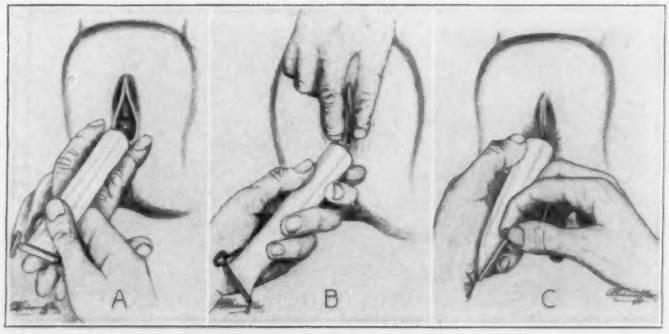

Fig. 5.—*A*, following exposure of the hymenal opening as shown in figure 1, the nozzle of the ointment tube, preferably the smallest size to start with, is gently inserted through the hymenal opening in a direction corresponding to the vaginal axis. Precision and steadiness may be gained by resting the barrel of the tube in the crotch of the index and the second finger as indicated. The nozzle (not the tube) should be warmed to body temperature. *B*, with the nozzle about one-third inserted, the tube is grasped with the left hand, and the fingers of the right hand are used to gently press toward the midline the fatty tissues about the vulva. *C*, the shoulder of the ointment tube is quite firmly approximated against these tissues, with resultant satisfactory occlusion of the outlet. The injection may now be begun. For this purpose, it is helpful simply to clamp a hemostat or a key on to the lower end of the tube and roll the tube around it, in expressing the ointment. The criteria of a successful technic are: first, that there be complete relaxation with a complaint by the child only coincident with positive intravaginal pressure; second, that there should be a liberal backflow of the ointment following the removal of the nozzle, and, third, that the ointment should appear on the pads for from twenty-four to forty-eight hours or more following the treatment.

of the infected field; (2) warm hydrous (instead of anhydrous) wool fat is used and petrolatum is introduced (i. e., the mixture is softer and has less fluid affinity), and (3) the antiseptic is too weak (figs. 4 and 5).

The most efficient ointment is plain anhydrous wool fat with 1 per cent silver nitrate incorporated with the least possible fluid solvent. Antiseptic dyes may be used if desired. This ointment is antiseptic, nonirritating, inexpensive and effective. The anhydrous wool fat is very sticky and tenacious and is not repulsed by the moist vaginal wall as is the ordinary grease base. Its firm consistency allows distention of the vaginal crypts under low pressure.

Prognosis and Schedule of Treatment.—The prognosis in the majority of early mild infections is good. A daily treatment for a week with a treatment every second day for another week will control the average case. For the stubborn cases, however, which comprise the majority seen in consultation, I have found the following schedule of value.[2] It is well, by the way, to state in the beginning that permanent results in the chronic infections should not be counted on under three months, and that, occasionally, it is virtually impossible to obtain an absolute cure. As a matter of fact, however, practically every stubborn case will yield to this method within a period of two months. The child should be treated every day for the first week, every second day for the two subsequent weeks and twice a week following this until such time as there is no local irritation or vestige of the discharge appearing on the pads or clothing. The period between treatments may then be experimentally prolonged, careful watch being kept of the pads or clothing. If no discharge appears within five or six days, the child should be treated again and watched for a longer period. When from ten days to two weeks have passed without evidence of discharge, there is little likelihood of relapse or recurrence. The child should, however, be watched at periods of from two to three weeks for the next month or so, and the case should be checked up occasionally thereafter.

Vaginoscopy should be carried out in all cases in which the introitus permits instrumentation without undue difficulty. If there is any notable difficulty, it is my practice not to perform vaginoscopy unless the condition does not react favorably to the vaginal treatment within two weeks.

No mention has been made of certain procedures which are occasionally necessary to the successful use of the method (i. e., hymenectomy, ethylene anesthesia). Associated proctitis, endocervicitis,

2. This schedule is in operation at the People's Free Dispensary, Children's Urological Clinic, Portland, Ore.

bartholinitis or skenitis should be suspected, particularly if conscientious vaginal treatment is not effective. Appropriate treatment should be used for pin-worms, foreign bodies, etc.

The purpose of this paper has been only to describe a rational, simple and highly effective method for the management of stubborn cases of primary vaginitis. A second detailed analysis and follow-up report of the excellent results obtained with this method in a large number of cases is being published elsewhere, but is not suitable for inclusion here.

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INFECTION OF THE EAR

IN CASES OF INFECTION OF THE GASTRO-INTESTINAL TRACT IN INFANTS *

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The question of the relationship between otitis media and gastro-enteritis, or so-called intestinal intoxication, has received considerable attention for a number of years from the pediatric as well as from the otologic standpoint. Within the past five years, however, a number of articles on this vital subject have appeared in the literature, with such variety of opinions that the reader was left in a state of doubt and uncertainty. Similarly, for a number of years, in the treatment of such patients at the Mount Sinai Hospital, considerable discussion and differences of opinion have arisen between the pediatric and the otologic attending staff. This indefinite state of affairs has prompted me to investigate these cases, both clinically and pathologically, and to attempt to arrive at some conclusions regarding the etiology, pathogenesis and treatment.

For the past fifty years and more, pathologic changes in the ears have been considered by some authors as etiologic factors responsible for the symptoms of intestinal intoxication. Thus Hartman,[1] in 1894, Preysing (quoted by Alexander [2]) and Gruening,[3] in 1910, and more recently Marriott,[4] Dean,[5] Floyd,[6] Alden and Lyman [7] and others [8] have

* Submitted for publication, May 12, 1931.

* From the Otological and Pathological Departments of Mount Sinai Hospital.

1. Hartman, Arthur: Die Mittelohrentzündung des Säuglinge, Deutsche med. Wchnschr. **20**:544, 1894.

2. Alexander, G.: Ohrenkrankheiten und Kindesalter, Leipzig, F. C. W. Vogel, 1927, p. 103.

3. Gruening, Emil: Pediatrics and Otiatrics, Arch. Pediat. **27**:732, 1910.

4. Marriott, W. McKim: Further Observations Concerning Nature of Nutritional Disturbances, Am. J. Dis. Child. **30**:577 (Oct.) 1925.

5. Dean, L. W.: Acute Otitis in Infants, Arch. Otolaryng. **6**:201 (Sept.) 1927.

6. Floyd, Mark L.: Masked Mastoiditis Simulating "Alimentary Intoxication," Arch. Otolaryng. **1**:411 (April) 1925.

7. Alden, Arthur M., and Lyman, Harry W.: Gastro-Intestinal Disturbances in Infants as Result of Obscure Infection in Mastoid, Tr. Am. Laryng., Rhin. & Otol. Soc., 1925, p. 67.

8. Jeans, P. C.: The Diagnosis and Importance of Sinusitis and Mastoiditis, Am. J. Dis. Child. **33**:357 (Feb.) 1927. Holsclaw, F. M.; Boehm, C. A., and Beerman, J. M.: Otitis Media and Mastoiditis in Infants Under Three Months of Age, Am. J. Dis. Child. **39**:747 (April) 1930.

attributed the gastro-intestinal symptoms to the otitic condition. In the treatment for this disease they were more or less in favor of radical surgical measures performed on the tympanum and mastoid, and they were guided more by the intestinal signs and symptoms and the general condition of the patient than by the otitic condition. On the other hand, a number of authors, Goppens, Steiner, Finkelstein (quoted by Stenger [9]), Heerman (quoted by Gomperz [10]), Morse, Abt (discussion of Marriott's paper [4]), Holt (Gruening [3]), Richards,[11] Wishart [12] and others, do not consider the aural condition per se as the etiologic factor. They are of the opinion that the otitic involvement is usually a concomitant condition or is secondary to the intestinal intoxication. Consequently, they advocated more conservative measures in the treatment.

The question naturally arises: Which of these two views is the correct one? An attempt to answer it was made by:

1. A review of the literature
2. Clinical study of such cases at the Mount Sinai Hospital
3. Pathologic study

REVIEW OF THE LITERATURE

In reviewing the literature, it was found that those authors who considered the otologic condition as primary based this opinion mainly on the following three reasons: 1. In a number of infants there was a history of infection of the upper respiratory tract antedating or appearing concomitantly with the intestinal symptoms. 2. A large percentage of infants who died of this condition showed purulent exudate in the middle ear and mastoid cavity. 3. A number of infants improved after myringotomy and mastoidectomy.

As regards the first point, namely, that in a number of infants there was a history of infection of the upper respiratory tract antedating or occurring simultaneously with the intestinal symptoms, it might be said that in a very large number of such cases there was no such history, while in others the infection of the respiratory tract appeared after the intestinal symptoms were advanced. Again, it is well known that infection of the upper respiratory tract is common in infants and is a

9. Stenger, P.: Akute Infektiös Krankheiten, in Denker, A., and Kahler, O.: Handbuch der Hals-, Nasen- und Ohrenheilkunde, Berlin, Julius Springer, 1926, vol. 7, p. 145.

10. Gomperz, B.: Mittelohr Entzündung im Säuglingsalter, Vienna, Josef Safár, 1906, p. 32.

11. Richards, Lyman: Mastoiditis in Acute Nutritional Disturbances, Arch. Surg. **18**:1774 (April) 1929.

12. Wishart, D. E. S.: Relation of Infection of the Ear and Infection of Intestinal Tract in Infants, J. A. M. A. **95**:1084 (Oct. 11) 1930.

precursor to many diseases; however, it is not considered the etiologic factor responsible for these diseases.

The line of reasoning given for the first point pertains also to the second; that is, a large percentage of infants who died showed purulent exudate in the middle ear and mastoid cavity. However, one important factor must be taken into consideration. Is the exudate in the middle ear and antrum found at autopsy of an infectious nature or is it an agonal change? Opinions on this question vary. While some authorities believe that the infectious process is genuine, others, like Preysing, Aschoff, Rinecker, Zaufel and Brunner and Heerman (all quoted by Gomperz [10]), believe that the exudate is physiologic. Preysing, for instance, found these suppurative-like masses in the new-born to be sterile. Aschoff believes that the exudate is the product of birth, that is, amniotic fluid, vernix caseosa and meconium, which make their entrance into the middle ear by way of the eustachian tube and sometimes remain there for a considerable length of time. He called this condition a "foreign body otitis." Zaufal and Brunner (quoted by Gomperz [10]) consider this exudate the remains of the normal breaking down of the embryonic tissue lining the tympanum. Heerman believes that the exudate is found in most debilitated children with lowered resistance, and he named this condition "otitis media concomitans." The criteria on which these opinions are based are not always given.

If one grants that the exudate in the middle ear is pathologic, one still must face the fact that this exudate is found not only in children who die of intestinal intoxication but in a large number of children who die from causes other than intestinal intoxication. From the figures of the various authors, exudate is found post mortem in about from 50 to 95 per cent of all infants up to 6 months of age.[10] It is also significant to note that there was nothing characteristic in the bacteriology of the intestinal intoxication as studied from postmortem cultures of the middle ear and antrum. The bacteriologic condition of the middle ear did not correspond with that of the intestinal tract. There was a preponderance of Streptococcus hemolyticus in the ears in these patients as well as in those who died of other causes.

With regard to the third point, that a number of infants improved after myringotomy or mastoidectomy, the following might be said: In some of these cases the aural condition was, in all probability, a concomitant and contributing factor to the general condition. Therefore, treatment for this condition was indicated. It is fully understood that the virulence and specificity of the infectious agent in the ear may vary in different localities and at different times. These factors undoubtedly play a rôle in the ultimate outcome of the disease. From the statistics offered in the literature and from our own experience, how-

ever, it was noted that a large number of infants succumbed after myringotomy and mastoidectomy. Also, a number of infants whose symptoms were apparently of the same severity and on whom myringotomy and mastoidectomy were not performed made uneventful recoveries.

The criteria advocated by those who favored operative intervention were based, not on the otitic condition, but on the general condition of the patient, and the decision often rested with the pediatrician and not the otologist. While some favored only myringotomy at first, others maintained that this procedure was inadequate, basing their opinion on the belief that the pus is frequently closed off in the antrum; they favored immediate mastoidectomy. The question arises: On which side is operation to be performed? "Operate on one side and if pus is not found the other side should be operated on, where it surely will be found." As a result, bilateral mastoidectomies were performed not infrequently. Apropos of this question, it is interesting to note that at one time pathologic changes in the middle ear were considered responsible for many cases of pyelitis and other lesions of the kidneys (Simmonds, quoted by Gomperz [10]). Many of these cases cleared up following myringotomy, and consequently myringotomies were performed at the least provocation. It was later observed that most of the infants recovered without myringotomy; the usual conservative treatment was then resumed. Recently, Wanner [13] maintained that myringotomy is seldom, if ever, indicated even in infants with measles or scarlet fever; and he, therefore, never performs it. He stated that he has never seen any intracranial complications as a result of waiting, and that the patients do just as well after spontaneous perforation as they do following myringotomy. In this view he is in accord with Southly. Thus one has an example of ultraconservatism.

CLINICAL STUDY OF CASES AT THE MOUNT SINAI HOSPITAL

In a very large percentage of the cases of intestinal intoxication for which the otologic service was called in consultation, the otoscopic findings were essentially negative throughout the entire illness. Occasionally pathologic changes in the middle ear were noted. These changes varied from slight congestion to marked bulging of the tympanic membrane. Less frequently, signs of postauricular involvement were present. The otitic signs occurred at no particular stage of the illness, appearing before, during or after the onset. Similarly, a number of infants have entered the pediatric and surgical wards for various other ailments who have had discharging ears on admission or have acquired this condition during their stay in the hospital. It was felt that the otitic

13. Wanner, F.: Die Parazentese, Ztschr. f. Laryng., Rhin. **19**:349, 1930.

condition in the intestinal, as well as in the other, cases was incidental or concomitant. That it may have been a contributing factor to the general condition of the patient seemed plausible.

Furthermore, it was noted that gastro-intestinal symptoms were seldom present in the patients admitted to the otologic service. This fact is also an indication against the association of the two conditions. Consequently, in the treatment for the otitic condition, the otologic service was guided by the aural signs and symptoms rather than by the general condition of the patient. In other words, the criteria for indications for myringotomy and mastoidectomy were the same in intestinal intoxication as in the other diseases.

Recently, Dr. Karelitz obtained favorable results in the treatment of a series of patients with intestinal intoxication on the pediatric service of Dr. Schick at the hospital. The therapy employed was nonsurgical, and consisted in the main of intravenous injections of dextrose. This article will be printed and a further clinical study of these cases from the otologic standpoint will be published by Dr. Maybaum within the near future.

PATHOLOGIC STUDY

In the pathologic study, I was unsuccessful in procuring the temporal bones for histologic sectioning in a large percentage of the patients who came to autopsy. In these cases, however, the middle ears and antrums were opened and investigated. In a general way, it was found that in about 50 per cent of them an exudate was present in the middle ear and antrum of either or both sides. In practically every case there was an absence of breaking down of the bony septums of the mastoid. Cultures were made in a number of such cases; the majority revealed the presence of the streptococcus. However, these findings differed in no way from those obtained in infants of the same age who died of causes other than intestinal intoxication. The impression gained was that when the exudate-like substance was present in the tympanum and antrum, it was an agonal or antemortem invasion.

The histologic data comprise a study in serial section of seven temporal bones. Clinically, in four of them the tympanic membranes were normal or slightly thickened and dull gray; in the remaining three, suppuration of the tympanum was present of two weeks', four weeks' and four months' duration. In three of the four cases that clinically showed relatively normal middle ears, histologically the middle ears and antrums were normal or slightly, if at all, inflamed (fig. 1). Purulent exudate was present in the antrum in one case. The presence of embryonic tissue and the degree of its recession were taken into consideration. In the three cases in which there was a discharge from the middle ear, clinically, the pathologic changes varied from a mild

purulent exudate in the tympanum and antrum (fig. 2) to a diffuse purulent labyrinthitis. The following pathologic changes were found: an abnormally thickened mucosa lining the tympanum and antrum, which in some areas was devoid of epithelium, while in others it was thrown into polypoid folds; granulomas on the tympanic membrane and

Fig. 1.—The upper picture shows a vertical section through the tympanum; the lower, a vertical section through the antrum. The tympanic and antral cavities are relatively normal. *A* indicates the antrum; *C*, the cochlea; *EAC*, the external auditory canal; *ESC*, the external semicircular canal; *FN*, the facial nerve; *M*, the malleus; *MSt*, the stapedius muscle; *PSC*, the posterior semicircular canal; *Pr*, the promontory; *St*, the stapes; *TC*, the tympanic cavity; *TM*, the tympanic membrane; *U*, the utricle; *V*, the vestibule.

Fig. 2.—The upper picture shows a vertical section through the tympanum; the lower, a vertical section through the antrum. A hyperplastic condition of the mucosa lining the tympanic cavity is present, and in the antrum, a granuloma is seen in the upper part of the tympanic membrane. *A* indicates the antrum; *C*, the cochlea; *DE*, the ductus endolymphaticus; *EAC*, the external auditory canal; *ESC*, the external semicircular canal; *FN*, the facial nerve; *FS*, the fossa subarcuata; *I*, the incus; *M*, the malleus; *MTT*, the tensor tympanic muscle; *PE*, the purulent exudate; *PSC*, the posterior semicircular canal; *St*, the stapes; *SSC*, the superior semicircular canal; *TC*, the tympanic cavity; *TM*, the tympanic membrane; *U*, the utricle; *V*, the vestibule.

secondary membrane; perforation of the drum; adhesive fibrous bands in the tympanum and antrum, and purulent exudate in the periantral cells. It is interesting to note that in all of these cases there was no evidence of necrosis of the bone. Incidently, even in the case of labyrinthitis, there was no evidence of destruction of the bone, the portal of entry to the labyrinth being the oval window.

The three cases in which clinically a middle ear suppuration was present deserve comment. In the first case, the suppuration was of four weeks' duration, while the intestinal symptoms were of six days' duration. Histologic study revealed the presence of a small amount of exudate in the tympanum and antrum; the mucosa was somewhat thickened. There was no evidence of disease of the bone. In the second case, the suppuration of the middle ear was of four months' duration, whereas the intestinal symptoms appeared one week prior to death. Histologic examination showed the presence of a large perforation of the tympanic membrane. Purulent exudate was present in the tympanic cavity and in Prussak's space; the ossicles were embedded in a mass of inflammatory tissue. The mucous membrane showed marked retardation in its recession, probably due to prolonged infection.

In these two cases, the pathologic observations in the tympanum and mastoid differed in no way from those of the usual middle ear infections. This opinion is supported by a comparative study in which histologic sections were made for a large series of infants who died of various diseases with and without an associated otitis media. It is possible that the otitic condition was a contributing factor for the intestinal symptoms, but it is hardly likely that it was the main etiologic factor. That the two conditions are concomitant seems more logical.

In the third case, involvement of the middle ear was of two weeks' duration, whereas the intestinal symptoms were of four weeks' duration. Histologically, the tympanum and the antrum showed a severe infection with a secondary labyrinthine involvement. Since the intestinal symptoms antedated the aural symptoms, the latter could hardly be held responsible for the former. As was stated previously, in the four cases in which clinically the middle ears were relatively normal, histologically few, if any, pathologic changes were noted.

One of these four cases is given as an example to demonstrate the inadvisability of performing myringotomy without definite physical signs. This infant had severe intestinal symptoms: vomiting after every meal, ten loose bowel movements daily, loss of weight and a continuous temperature of about 101 F. Both tympanic membranes were thickened, but the landmarks were discernible. In view of the progressive intestinal signs, the question of myringotomy arose, but it was decided

to delay this procedure for twenty-four hours. In the interim, however, the signs temporarily improved. If the myringotomy had been performed, the improvement would have been attributed to this procedure. The child finally succumbed. Histologic examination showed no evidence of any inflammatory changes in the middle ear (fig. 1). The temporal bone of the opposite side, which was not sectioned, also showed normal findings on gross examination.

SUMMARY AND CONCLUSIONS

Cognizance is taken of the fact that although it is difficult to draw any conclusions from the limited number of cases at my disposal, the findings were nevertheless significant. While it is the rule for cases of intestinal intoxication to run their course without aural involvement, at times the latter condition may co-exist, appearing before, during or after the onset of illness. Consequently, the pathologic picture of the middle ear and mastoid will vary, depending on the presence and the degree of the otitic involvement. There are no specific anatomic pathologic changes in the middle ear or mastoid that are characteristic for cases of intestinal intoxication.

It is fully understood that infectious agents may vary in their specificity and virulence with regard to time and location, so that no hard and fast rules can be laid down. However, from a review of the literature and from a clinical and pathologic study of the cases, the preponderance of evidence favors the view that the otitic condition is not the etiologic factor responsible for the intestinal intoxication. An infection of the ear may influence the course of the illness, and it should be treated accordingly. The causative factors, however, must be looked for elsewhere. Consequently, in the treatment, cures cannot be hoped for by operations on the middle ear and mastoid process.

Dr. Friesner, Dr. Klemperer and Dr. Schick assisted me in the course of this work.

GAUCHER'S DISEASE

A CLINICAL STUDY, WITH SPECIAL REFERENCE TO THE ROENTGENOGRAPHY OF BONES *

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In spite of the comparative rarity of the condition, Gaucher's disease has of late aroused a considerable amount of interest, chiefly because of a rather unique pathologic process in the bone. From the present state of knowledge concerning its pathogenesis and evolution, we may define the condition as a familial, chronic, constitutional, nonhereditary disease of metabolism, which is characterized by the deposition of cerebroside kerasin in certain cells of the reticulo-endothelial system. Clinically, it shows splenohepatomegaly, without ascites, occasional lymphadenopathy, subicteric pigmentation of the exposed parts of the skin, pinguecula-like thickening of the ocular conjunctiva, hemorrhagic diathesis, unique changes in the bones, a hypochromic type of anemia, slight but early leukopenia, frequent thrombocytopenia and spastic irritative contractions and tremors of a central type. The disease is considered rare, although the increasing knowledge of the condition is causing more frequent recognition of it in recent years. A comprehensive tabulation of all reported cases in the literature by Hoffman and Makler [1] reveals nearly ninety cases on record. There are

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1. Hoffman, S. J., and Makler, M. I.: Gaucher's Disease: A Review of the Literature and Report of a Case Diagnosed from Section of an Inguinal Gland, Am. J. Dis. Child. **38**:775 (Oct.) 1929.

twenty-four cases published which their table does not include, in addition to the three cases here reported.[2]

The condition was originally described in detail as "primitive endothelioma of the spleen" by the eminent French dermatologist, Philippe Charles Ernest Gaucher, in 1882, but his idea of this disease as a form of neoplasm was soon abandoned. The disease remained unclassified for nearly thirty years, and many reports of conditions closely resembling but quite different from Gaucher's disease were published under its name. Since the publication, however, of a series of accurate studies by Brill, Mandlebaum, Libman and Downey, knowledge of this disease has materially advanced. According to these investigators, the condition is systemic, probably due to a disturbance in metabolism, characterized by the presence of the so-called large Gaucher cells, containing complex substance in their cytoplasm with eccentrically placed nuclei, in all the organs of the body where the elements of the reticuloendothelial system are found. Thus the sinus endothelium and reticulum cells of the splenic pulp, Kupffer's stellate cells and the clasmatocytes of interlobular connective tissues of the liver, the reticular and endothelial cells of sinuses in the lymph nodes, as well as the adventitial cells

2. These cases are published in the following articles: Mills, H. B.; Asnis, E. J., and Babcock, W. W.: Report of a Case of Splenomegaly, New York M. J. **113**:589, 1921. Bang, H.: Bantis sygdom (forme-Gaucher) xanthoma universale, Førhandl. Dansk med. Selskab, 1922-1923, p. 64. Meulengracht, E.: Et tilfaelde af Gaucher's splemegali, Ugesk. f. læger **87**:661, 1925. Junghagen, S.: Röntgenologische Skelettveränderungen bei Morbus Gaucher, Acta radiol. **5**:506, 1926. von Müller, F.: Problems of Disease of the Joints, Arch. Int. Med. **40**:399 (Oct.) 1927. Fischer, A. W.: Das Röntgenbild der Knochen, besonders das Femur in der Diagnose des Morbus Gaucher, Fortschr. a. d. Geb. d. Röntgenstrahlen **37**:158, 1928. Humperl, H.: Ueber die pathologisch-anatomischen Veränderung bei Morbus Gaucher im Säuglingsalter, Virchows Arch. f. path. Anat. **271**:147, 1929. Milch, H., and Pomeranz, M.: Bone Changes in Gaucher's Splenomegaly, Ann. Surg. **89**:552, 1929. Welt, S.; Rosenthal, N., and Oppenheimer, B. S.: Gaucher's Splenomegaly, with Especial Reference to Skeletal Changes, J. A. M. A. **92**:637 (Feb. 23) 1929. Bonta, M. B.: Splenomegaly in Gaucher's Disease, Proc. Staff Meet., Mayo Clin. **4**:262, 1929. Frick, P., and Friedrich, G.: Morbus Gaucher im frühen Kindesalter, Arch. f. Kinderh. **90**:1, 1930. Moncrieff, A.: The Infantile Type of Gaucher's Disease, Arch. Dis. Child. **5**:265, 1930.

Since the foregoing was written, the following additional reports on Gaucher's disease have come to our attention: Kirklin, B. R., and Hefke, H. W.: Roentgenographically Demonstrable Changes in Bone in Gaucher's Disease, Am. J. Roentgenol. **24**:258 (Sept.) 1930 (one case). Melnikoff-Razvedenkoff, M. F.: Gaucher's Splenomegaly in the Ukraine, Ukrain. m. visti **6**:71, 1930 (not available). Antonow, A.: Zur pathologischen Anatomie der Gaucher-Krankheit, Frankfurt. Ztschr. f. Path. **41**:26, 1931 (with a review of eight cases reported in the Russian literature). Barchasch, P. A., and Gurin, B. I.: Klinik und intravitale Erkennung des Morbus Gaucher, Folia haemat. **45**:43, 1931 (two cases).

and the littoral cells of vascular walls everywhere, are usually changed into these "storage" cells, replacing and distorting the normal anatomic structure of these organs.

These cells show considerable variation in size, according to Mandlebaum,[3] the average diameter being from 20 to 40 microns, but occasionally cells of huge size, from 70 to 100 microns, are seen. They are round or oval when isolated, but when large compressed areas are found the cells are usually fused into long strands or united as syncytial masses. They show a strong affinity for acid stains, which bring out clearly a network of fine fibrils running in a wavy parallel course in the direction of the longitudinal axis of the cell (fig. 1). This gives to the cell its streaked or wrinkled appearance, but when the cell has been cut transversely to the main direction of the fibrils, the cytoplasm appears granular or stippled. In many of the cells one sees irregularly shaped or elongated, colorless areas bounded by the fibrils which have been crowded apart. The shape of these colorless spaces is an important point of distinction between the Gaucher cells and the cells seen, for example, in lipoid histiocytosis, diabetic lipemia or in animals fed with cholesterol. In the latter conditions, the colorless spaces or vacuoles are rounded and contain a lipoid substance that gives a positive reaction with such fat stains as sudan III, nile blue or Smith-Dietrich stain.

The chemical analysis of the specific substance stored in Gaucher cells has been made by several workers. Mandlebaum found that by making various quantitative estimations on the extractives obtained by means of alcohol, ether and chloroform from the thoroughly dried formaldehydized and fresh spleen in his three cases, the cholesterol-lecithin fraction varied from 46 to 80 per cent, and in one case the cholesterol figure was 51, which is much higher than in the other two cases in which it was 5.4 and 7.5, respectively. The actual identification of the Gaucher substance was accomplished by Lieb,[4] who by treating the 40 degree fraction of extractives by cold saturated aqueous solution of corrosive mercuric chloride obtained a voluminous gelatinous precipitate. This precipitate was redissolved in alcohol, freed from mercury by means of hydrogen sulphide while heating, and filtered hot. A gelatinous precipitate appeared in the filtrate on cooling, which when decolorized with animal charcoal gave a semblance of cooked egg albumin. Under a microscope this material shows a crystalline form.

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3. Mandlebaum, F. S.: Two Cases of Gaucher's Disease in Adults: A Study of the Histology, Biology and Chemical Findings, Am. J. M. Sc. **157**:366, 1919.

4. Lieb, H.: Cerebrosidspeicherung bei Splenomegalie, Typus Gaucher, Ztschr. f. physiol. Chem. **140**:305, 1924. Epstein, E., and Lorenz: Beitrag zur Chemie der Gaucherschen Krankheit, Biochem. Ztschr. **145**:398, 1924. Bloom, W., and Kern, R.: Spleens from Gaucher's Disease and Lipoid-Histiocytosis. Chemical Analysis, Arch. Int. Med. **39**:456 (March) 1927.

On hydrolysis with acid, a slight reducing power was observed. From all the properties demonstrated by various tests, the substance was finally identified as a cerebroside called kerasin, the empiric formula of which, according to Rosenheim, is C_{47} H_{91} O_8 H + H_2O. It is soluble in warm alcohol but insoluble in ether. It is a sphingogalactoside, which on acid hydrolysis yields lignoceric acid, sphingosine and d-galactose.

Fig. 1 (case 1).—Gaucher cells from the section of the spleen removed from the oldest patient. The majority of these cells are from 20 to 40 microns in diameter, with finely reticular cytoplasm and one or more nuclei. A few of the larger cells appear to be multinuclear giant cells.

This observation has been repeated and confirmed by Epstein and Lorenz and Bloom and Kern.

Concerning the origin of Gaucher cells in the various organs affected, there has been much difference of opinion. Some have regarded the

cells as derived from the endothelial cells, while others have held the origin to be the reticulum cell of the lymphatic-hematopoietic system. There are a few authors who believe in a double origin. This problem has received careful study by Mandlebaum and Downey,[5] who noted that in the lymph nodes in which the involvement is far advanced, the follicles or remnants of follicles were always surrounded in the center by a ring or a wall of large cells. The process began in a small group of large cells in the germinal center or at the periphery of the follicle. These cells spread outward from the germinal center. In this way a follicle was gradually replaced by Gaucher cells, and the lymphocytes gradually disappeared. The significant fact was that the Gaucher tissue occurred in the regions in which the reticulum showed distinct evidence of hypertrophy. Usually, the changes in the spleen and the liver are so advanced that the exact steps of pathogenesis are not clearly demonstrated, but in a lymph gland in which the pathologic processes are just beginning, as in the studies made by Mandlebaum, the origin of the large cells from the reticulum is readily recognized.

CLINICAL MANIFESTATIONS

As to clinical manifestations of the disease, the more important symptoms may be summarized. The slow but progressive enlargement of the spleen is the most characteristic, and the concomitant growth in the size of the liver and consequent abdominal distention are the signs of illness that first attract the attention of the parents. There is only occasionally a dull pressure pain, and as a rule no ascites. There may be generalized lymphadenopathy, but this is never marked. The color of the skin, especially on the exposed parts, presents a peculiarly dull brownish or at times slightly yellowish, but never generalized icterus, pigmentation, as is seen in the usual types of jaundice. In older patients, particularly in adults, a wedge-shaped thickening of the ocular conjunctiva with its base toward the corneal margin may be present, but in young children and infants, this is seldom if ever seen. There is a tendency to bruise easily, and the occasional presence of petechiae or even of suggillations may be noted. Bleeding from the nasal and oral mucous membrane is frequently encountered and may be very distressing owing to its persistence. Hemoptysis, hematemesis and menorrhagia have been reported. The blood picture is fairly characteristic, although not absolutely unique or pathognomonic. The red cells are slightly reduced in number, the usual count ranging between 3,000,000 and 4,000,000, while the hemoglobin may be as low as from 35 to 50 per cent, indicating a chlorotic or hypochromic type of anemia. There is

5. Mandlebaum, F. S., and Downey, H.: The Histo-Pathology and Biology of Gaucher's Disease (Large-Cell) Splenomegaly, Folia haemat. **20**:139, 1915.

usually a slight but early leukopenia, the number of leukocytes ranging between 3,000 and 12,000, with practically a normal differential count. There is no tendency for erythroblastemia or reticulocytosis. The platelet count may be low, and in many cases it is reduced to about 50 per cent of the normal value. The results of the chemical examination of the blood has been reported in only a few cases, in which the total nonprotein nitrogen, calcium, creatinine, uric acid and phosphorus were normal. In a few instances, the blood sugar showed a value of about 125 mg. per hundred cubic centimeters, or a slight hyperglycemia. The amount of phosphatides, cholesterol and total fatty acids is also normal or may be lower than normal, this fact differentiating Gaucher's disease from Niemann-Pick's disease.

The cases here reported show two interesting clinical findings, one referable to the nervous system and the other to typical bone changes. There are very few references in the literature to nervous manifestations. In four cases of Oberling and Woriger [6] there were opisthotonos, spasticity, strabismus and pathologic reflexes. They applied the term of "progressive decortication" to this syndrome. From the history and course of our cases, it is apparent that the two older patients showed almost from the very outset a syndrome consisting of converging strabismus, difficulty in focusing of vision, generalized spasticity especially noticeable in the extremities, bilateral ankle clonus, convulsive seizures, painful and stiff neck, coarse uncontrollable tremors and increased muscle and tendon reflexes, without Babinski or Oppenheim signs. These symptoms were rather constant and marked during the waking hours, but apparently lost during sleep. They were controlled with difficulty, or not at all, by the usual sedatives and hypnotics unless employed in large doses.

As to the interpretation of these phenomena, it may be possible to conceive of the extension of Gaucher cells into the tissues of the central nervous system or of the phagocytosis or storage of Gaucher substance in the reticulo-endothelial elements of the brain and the spinal cord exerting an irritative effect by pressure on the cortex and the fibers, in the same manner as an unabsorbed blood clot following intracranial hemorrhage may act in producing a state of spasticity by compression of the motor areas of the brain. In fact, a neurologic consultation brought out the idea that the nervous symptoms were due to a blood clot, from brain hemorrhage, in the cerebrum. From the fact that the optic disk showed no evidence of being choked but a slight degeneration, with no nystagmus or ocular palsy, and with the intact sensorium, the neurologist made a diagnosis of hemorrhagic encephalitis as a probable

6. Oberling, C., and Woriger, P.: La maladie de Gaucher chez le nourrisson, Rev. franç. de pédiat. **3**:475, 1927.

lesion in producing this train of symptoms. These nervous symptoms continued to become aggravated during the last stage of illness, until the patients became total invalids with reference to the use of their arms and legs, and the defect in vision almost approached the state of complete blindness.

The bone changes in Gaucher's disease have been mentioned by older writers, and, according to the tabulation of reported cases by Hoffman and Makler, 22 per cent of all cases gave a hint in their history of some bone involvement. Pick,[7] in his monograph entitled "Skelettform des Morbus Gaucher," brought out very concisely the osseous form of this disease. Since his publication, typical changes have been noted in practically all the bones of the body in the person affected with Gaucher's disease. Our cases demonstrate in a striking way many of these bone changes.

In the history of patients with bone involvement, there is usually a complaint of pains in the bones or sometimes in the joints. In the case reported by Gaucher himself, there was a history of bone pain. This pain may be merely a vague, unlocalized and occasional complaint, or it may be a constant dull pain. Sometimes there is a definitely localizable pain in the joints, the most frequent site involved being the hip and occasionally the knee joints. It may sometimes manifest itself in a sense of numbness or stiffness of the extremities, indicating the involvement of the ends of the long bones and the joints, where the pathologic process is at its height. With these joint pains, there is generally decided difficulty in walking. This is often attributed to the size of the abdomen. The real nature of the trouble lies in the bone involvement at the epiphysis. The stunted appearance often observed in patients suffering from Gaucher's disease may be due to these changes. Cases of extreme degrees of dwarfism or infantilism, associated with mental subnormality, have been reported.

ROENTGENOLOGIC EVIDENCE IN THE BONES

The roentgenologic examination of bones in Gaucher's disease has furnished a large amount of information as to the nature of the changes in the skeletal system. By this method, one is able in many instances to offer definite and positive data which aid in the antemortem diagnosis of the disease. Klercker[8] and Junghagen[9] were the first to make a complete study of these bone changes by this method. Following them

7. Pick, L.: Die Skelettform (ossuäre Form) des Morbus Gaucher, Jena, Gustav Fischer, 1927 (forms no. 17, vol. 4, Veröffentl. a. d. Kriegs- u. Konst.-Path.).

8. Klercker, K. O.: Beiträge zur Kenntnis des Morbus Gaucher, besonders im klinischer Hinsicht, Acta pædiat. **6**:302, 1926-1927.

9. Junghagen, S.: Röntgenologische Skelettveränderungen bei Morbus Gaucher, Acta radiol. **5**:506, 1926.

there are the studies by Cushing and Stout,[10] Santee,[11] Fischer [12] and Welt and her co-workers.[13] There is a decided similarity in all the pathologic changes of the bone that occur in cases of Gaucher's disease, as is shown in figures 2, 3 and 4, in which a comparison of the cases reported with ours is attempted by means of pen and ink tracings of roentgenograms.

Of all the bones of the body, the femur shows the most typical changes. In an early case, the femur may be the only bone that demonstrates the changes from the standpoint of the roentgenogram. The change in the lower end, most frequently seen, consists of the presence of areas of rarefaction of varying sizes, which in some cases are intermingled with areas of sclerosis. There results a picture often described as "worm-eaten" or "punched-out." The cortex is thin and extremely irregular, especially toward the middle portion of the diaphysis. One or more growth arrest lines may be visible just shaftward to the epiphyseal edge. The most interesting change, however, is that of the bilateral swelling or fulness of the shaft just above the condyles. This is more pronounced on the medial side. The fusiform expansion may be so marked that the normal contour of the distal end of the femur, with a concave flaring of condyles, may be transformed into the shape of an Erlenmeyer flask or have a club-shaped appearance (fig. 2). This distorted and abnormal configuration of the lower third of the femur has been noted with such constancy that one may regard it, when properly correlated with other findings, as a diagnostic sign of this disease. Welt, Rosenthal and Oppenheimer regard the sign as very important, and stated that "the definite expansion of the lower third of the femur, especially toward the internal condyles obliterating the normal contour, should be looked for as an early roentgenologic sign of the disease, whereas the mottled, worm-eaten appearance is probably roentgenologic evidence of a more advanced stage of involvement."

The upper end of the femur, including the neck and the head, also often shows marked changes in the majority of cases on record. In our cases, the hip joint symptom was one of the outstanding items in the history. The roentgenologic examination reveals a marked degree of osteoporosis and extensive areas of rarefaction, mingled with those of

10. Cushing, E. H., and Stout, A. P.: Gaucher's Disease, Arch. Surg. **12**:539 (Feb.) 1926.

11. Santee, H. E.: Gaucher's Disease, with Report of Two Cases in Brothers, Ann. Surg. **86**:707, 1927.

12. Fischer, A. W.: Das Röntgenbild der Knochen, besonders des Femur in der Diagnose des Morbus Gaucher, Fortschr. a. d. Geb. d. Röntgenstrahlen **37**:158, 1928.

13. Welt, S.; Rosenthal, N., and Oppenheimer, B. S.: Gaucher's Splenomegaly, with Especial Reference to Skeletal Changes, J. A. M. A. **92**:637 (Feb. 23) 1929.

condensation. One very important finding is the presence of a pathologic fracture through the surgical neck of the right femur. The fracture caused the neck and the head of the bone to bend downward so that the angle made by the axis of the neck and that of the shaft is almost a right angle, whereas in the normal bone, this angle is always obtuse. The same finding as to the angulation of the two axes is seen on the left, although no fracture is demonstrable on this side. The

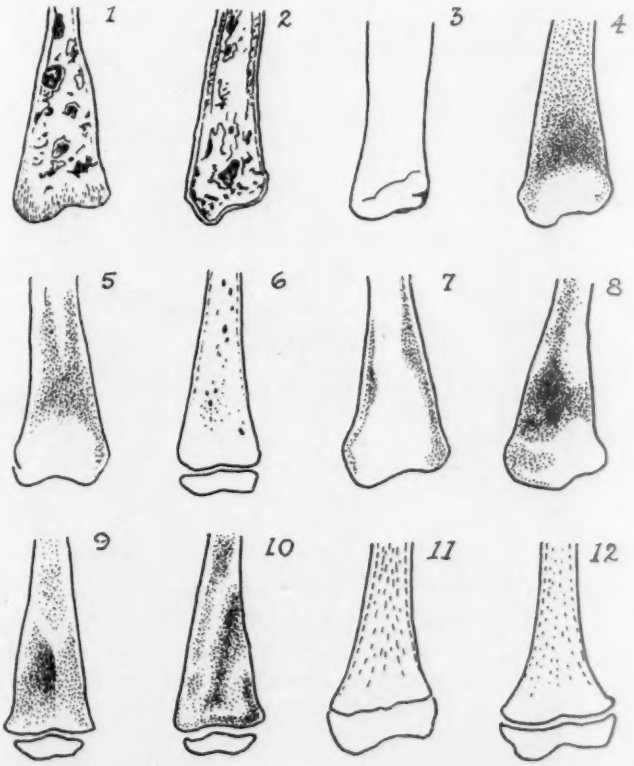

Fig. 2.—Changes seen in the lower ends of the femur in the cases of the following authors: (1) Pick, case 14; (2) Pick, case 19; (3) Howland and Rich; (4) Fischer, case K, right; (5) Fischer, case Tr.; (6) Junghagen; (7) Fischer, case, left; (8) Welt, case 2; (9) authors, case 1, left; (10) authors, case 1, right; also in (11) a normal femur with a broad end in an adult, and (12) a normal femur with a flaring end in a 9 year old child. The dotted areas represent the areas of rarefaction as seen in the roentgenograms.

head of the femur often shows flattening, with areas of rarefaction. All cases show a decidedly deformed appearance of the shape of the head, resembling the conditions found in chronic osteomyelitis, Perthes' disease or tuberculous coxitis. The portion just below the neck also

shows a mottled appearance, owing to the juxtaposed areas of rarefaction and condensation, with irregularities in the thickness of the cortex (fig. 3).

The same changes are seen in practically all other long bones, especially the humerus, tibia, fibula, radius, ulna and the ribs, perhaps in the order named from the standpoint of the degree of pathologic change. The pelvis also is frequently involved.

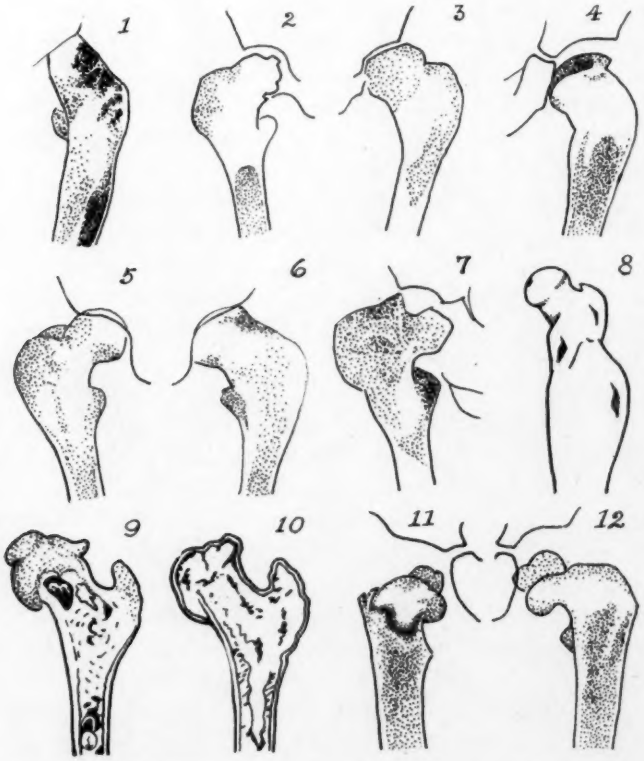

Fig. 3.—A comparative study of the head, neck and upper end of the femur copied from roentgenologic and pathologic case reports by various authors: (1) Welt, case 3; (2) Welt, case 2, right; (3) Welt, case 2, left; (4) Junghagen; (5) Santee, right; (6) Santee, left; (7) Cushing and Stout; (8) Howland and Rich; (9) Pick, case 14; (10) Pick, case 19; (11) authors' case 1, right, and (12) authors' case 1, left.

Of the other bones of the body, the most interesting changes are seen in the vertebrae. Since Pick described in detail the changes found in his cases, the condition has been looked for by subsequent observers, and Junghagen demonstrated roentgenologically the compression of the spinal column due to the deformity of some of the vertebrae. A com-

parison of these changes is shown in figure 4 in which pen and ink tracings of the roentgenograms demonstrate the pathologic process in question. Howland and Rich [14] reported a case in which the disease process invaded the lumbar vertebrae rather extensively, together with other bones of the body. Roentgenologically, our cases do not demonstrate the changes in the vertebrae.

When any portion of the spinal column is affected, there is usually produced a compression fracture of the spine due to gibus formation. The Gaucher cells are present in nearly all the bones of the column, but the actual deformity and compression fracture may be limited in

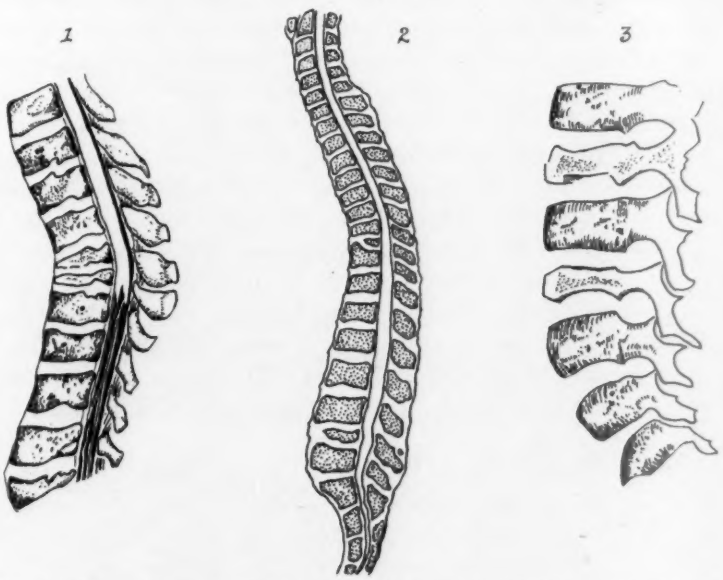

Fig. 4.—Bone changes in the vertebral column: 1. Pick's case 14, showing the right half of the vertebral column, with gibus formation at dorsal 11 and 12 and compression of the lumbar 5. The Gaucher cells have invaded practically every vertebra in this case. 2. Pick's case 19, showing the median longitudinal surface, with gibus formation at dorsal 9 and pathologic involvement of lumbar 4. The intervertebral disks are somewhat distorted but remain intact. 3. The lumbar vertebrae in Junghagen's case, showing the compression of the second and fourth, and involvement of others in lesser degree.

number. One important point emphasized by Pick is the fact that in Gaucher's disease the intervertebral disks are usually intact, in spite of the extreme degree of bone destruction, a point that differentiates the condition from tuberculous spondylitis.

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14. Howland, J., and Rich, A.: Gaucher's Disease with Extensive Involvement of the Bones and Invasion of the Spinal Canal, Tr. Am. Pediat. Soc. **34**:42, 1924.

The skull bones are not immune to the invasion of Gaucher cells, although actual observation is limited to one case reported by Pick,[15] who gives a good description as well as an illustration showing the interior of the calvarium, where it is found that the diploe is filled with a Gaucher cell mass and the inner surface of the parietal bones contain symmetrically placed yellowish spots of these cell nests.

The changes in the bones, and particularly in the marrow, were first noted macroscopically by Risel,[16] who described the spongiosa at the upper and lower ends of the humerus dotted with rather small, thick, whitish areas arranged in a stellate form either in nodes or streaks or in a netlike manner. Microscopically, these nodes or streaks contain the same large cells as those observed in the spleen and lymph glands. They are of the same size and show a similar content. The same observations were made by Brill, Mandlebaum and Libman, Rusca, Kraus and Evans, all of whom saw "some yellow or white spots" in the dark red marrow. These spots represent the accumulation of Gaucher cells, which for the most part retain the same shape found in other organs of the lymphatic-hematopoietic system, but where they are compressed by unyielding walls, as between the trabeculae of spongiosa, they may assume an elongated and spindle form, often resembling the fibers of smooth muscle. These masses of Gaucher cells may be intermingled with lymphoid cells, and in hematopoietic tissues of the myeloid areas, they are intimately mixed with red blood cells. Often the cells cling to the reticulum fibers of the marrow, the fibers forming a part of the cell contour.

When the disease is long continued, the accumulation of Gaucher cells and the consequent pressure on the surrounding tissues may cause necrosis of the spongiosa, leading to the rarefaction and irregular lining of the cortex. When such necrosis takes place at the epiphysis, which is the common site of the most extensive involvement, pathologic fractures may result, as illustrated in our first case. It is this necrotic process that causes the gibus formation in the vertebral column leading to compression fracture. If the tissue adjoining the joints is invaded, there may result a form of chronic secondary arthritis, after the joint surface is broken through. The intervertebral disks never become deformed, although they may be filled with Gaucher cells and hold the deformed vertebrae in their substance.

The diagnosis of Gaucher's disease has become comparatively simple, since the studies on various aspects of the disease have been established

15. Pick, L.: Der Morbus Gaucher und die ihn ähnlichen Erkrankungen, Ergebn. d. inn. Med. u. Kinderh. **29**:519, 1926.

16. Risel, W.: Ueber das grosszellige Splenomegalie (Typus Gaucher) und über das endotheliale Sarkom der Milz, Beitr. z. path. Anat. u. z. allg. Path. **46**:241, 1909.

with a fair degree of certainty. When the disease is well developed, the characteristic symptoms are present. The roentgenologic examination of the skeletal system should never be omitted in all suspected cases, for it may be the deciding factor in a correct diagnosis. Under certain conditions, biopsy of an accessible organ may be undertaken. The splenic puncture, which has been successfully employed as a diagnostic procedure, is not a universally commendable method, because of certain serious dangers attending it. There are a few conditions in infancy and childhood that simulate Gaucher's disease, and these must be carefully differentiated.

The disease is essentially chronic, and in cases in which the involvement of organs is moderate, life may be prolonged to a fair age. In these patients, however, the resistance to infection is decidedly low; hence they are frequently victims of intercurrent infections, which form the greater percentage of causes of death in these cases. Although it is usually stated that the disease in itself is seldom a cause of death, it is quite possible to conceive of death following an extreme cachexia directly referable to the pathologic process.

Splenectomy is the only method of treatment. It was first advocated by Eppinger in cases in which alleviation of discomfort due to splenic tumor is demanded. Surgical intervention, however, gives only temporary relief and has no value as a cure for the disease.

REPORT OF CASES

The three cases that form the basis of the present study occurred in a family of six children whose parents are natives of Japan living in California. Aside from the fact that the grandmother of the children on the father's side gave a positive Wassermann reaction there was nothing of significance in the family history. The first, the second and the last child were the patients under consideration.

CASE 1.[17]—*History.*—The oldest patient, a girl, born on Dec. 19, 1921, was a full term baby, normally delivered. She was breast-fed for seven months and was then fed Borden's condensed milk until she was a year old. She had been sick a good deal of her life, with a history of frequent colds and poor eyesight, having much trouble in focusing objects. In July, 1923, she had bronchopneumonia, and in February of the following year, she was treated for whooping cough. In December, 1924, she had lobar pneumonia. At that time the abdomen was distended, but there was no ascites. The liver was palpable, and the spleen could be felt at the level of the umbilicus. There was no jaundice, although the skin had a muddy appearance.

17. Case 1 of our series was reported by H. Hara and F. Guido in 1926 (California & West. Med. **25**:215, 1926), but a wrong impression is conveyed as to the final outcome, as these authors failed to follow the course until termination. Dr. Hara secured the past history of this case.

In January, 1925, acute edema of the left thigh developed, extending from the labia majus to below the knee. This the family physician believed was due to enlarged intra-abdominal glands causing an obstruction of the venous return. The child was unable to walk because of pain. The liver was enlarged fully 5 cm. below the costal margin and the spleen extended 3.5 cm. below the umbilicus and 5 cm. to the left of the midline. The swelling of the thigh disappeared in two weeks, with no recurrence. In March, 1925, she was taken to the Children's Hospital of Los Angeles for further observation. At that time the Wassermann reaction of the blood was reported 2+, but this was the only time that it was positive.

Examination at that time revealed an irregularly shaped tumor on the left side of the abdomen, extending to within 1 cm. of the median line and about 2.5 cm. below the crest of the ilium. No ascites was present. There were many fine petechiae over various parts of the body and larger hemorrhagic spots over the right knee. No general adenopathy was noted. Several intramuscular injections of arsphenamine were given, but the patient grew gradually worse; antisyphilitic treatment was discontinued, and the patient left the hospital in three weeks. Through 1925 the disease continued to progress, and the child grew gradually weaker, having frequent small hemorrhages from the nose and gums. She became very dull and would not play. The abdominal enlargement progressed to such an extent that she was unable to walk.

The patient entered the Los Angeles General Hospital on December 22, 1925, with a diagnosis of bronchopneumonia and splenomegaly. The temperature on admission was 102 F. No definite history could be obtained from the parents, save that the child had been sick for the few days preceding, with fever, and that an abdominal enlargement had been present for over a year.

Examination.—Physical examination on admission revealed a Japanese girl about 4 years of age, who apparently was acutely ill. The child was very dull, coughed a little and did not complain on being examined. She looked dull and quite acutely ill. She paid little attention to her surroundings. The scalp was normal. There was dried impacted cerumen in both ears, but the drum membranes were normal. No icterus was noted in the sclera of the eyes, but marked paleness of the conjunctivae was present. No evidence of any conjunctival thickening was seen. The media were clear, the disks well defined and the vessels normal. There was some crusted blood at the external nares, owing, evidently, to recent hemorrhage. The gums were normal, and there was no evidence of bleeding from them. The tonsils were hypertrophied, and a large amount of adenoid tissue was present. In the neck, there were many small, discrete, firm, but not tender, glands palpable, the posterior superficial glands on the left side being most numerous. The chest wall showed no rachitic rosary. Respirations were rapid, and there was an expiratory grunt; the respiratory rate was 40 per minute. There were no areas of dulness, but many moist râles could be heard over both lungs. The heart was normal in area and sounds. The pulse was regular in rhythm, but increased in rate.

The abdomen was markedly distended, being most prominent on the left side. There was no ascites. The spleen filled the entire left side of the abdomen and extended below the umbilicus and into the right iliac fossa. The lower margin of the spleen was lost beneath the brim of the pelvis. Three splenic notches were definitely palpable and sharply outlined. The spleen was firm and not tender. There were many discrete, firm, nonpainful glands in both groins. The genitalia were normal. No epitrochlear or axillary glands were palpable. Muscular tone was diminished. The reflexes were normal. It was difficult to determine whether there

was any pigmentation of the skin because of the natural color of the child. There was marked perspiration at all times. The patient's weight was 32 pounds and 10 ounces (14.8 Kg.).

Course.—After admission, the child was found to have a positive diphtheria culture, and was transferred to the contagious ward. There were no signs of clinical diphtheria. Ten thousand units of a diphtheria antitoxin, however, was given intramuscularly as a prophylactic. There was slight epistaxis at this time.

On the following day, December 25, a temperature of 104 F. developed, with bronchial breathing over various areas of the lungs, dyspnea and a respiratory rate of 42. The condition of the child remained unchanged for two weeks; her appearance was deeply toxic and the temperature ranged between 100 and 104 F. It then began to recede gradually, and by Jan. 15, 1926, convalescence was well established, and the feasibility of a splenectomy was considered. Up to this time, the patient had had a slight nosebleed every day, but the gums had never bled. She perspired freely, the sweat having a sweetish odor.

The Wassermann reactions of the blood were negative on all occasions except one. The urine was acid in reaction, with a specific gravity of 1.022, and contained

TABLE 1.—*Blood Count in Case 1*

Date	Red Blood Cells in Millions	White Blood Cells in Thousands	Hemoglobin, per Cent (Tallqvist)	Differential Count, per Cent				
				Lymphocytes		Polymorphonuclear Neutrophils	Mononuclears	Platelets
				Small	Large			
1/12/25	4.700	8.00	78	22	15	63	..	.....
3/30/25	4.250	10.10	..	..	..	..	..	.....
4/ 2/25	.....	4.85	..	46		54	..	1,500,000
12/23/25	2.980	7.00	30	29	7	59	5	.....
12/28/25	2.440	8.20	30	19	5	75	..	.....
1/ 6/26	2.344	6.45	25	56		40	4	993,000

no albumin, sugar or acetone, but a few epithelial cells. The icteric index was 10. The fragility test showed initial hemolysis at 0.46 per cent sodium chloride, and complete hemolysis at 0.28 per cent. Chemical examination of the blood showed 108 mg. of sugar per hundred cubic centimeters and 35 mg. of nonprotein nitrogen. The bleeding time was one minute and forty-five seconds. The blood count on stated dates is given in table 1.

From the history, physical examination and laboratory finding, a diagnosis of Gaucher's disease was made, and operation was performed by Dr. C. T. Sturgeon on January 22. The child was in very poor condition and bled profusely from the nose during the operation. The abdomen contained no fluid, the spleen filled the entire left side of the abdomen and was attached by firm adhesions to the diaphragm. The liver was enlarged to four fingerbreadths below the costal margin. There were no adhesions, and the capsule was normal. The spleen was removed, as well as a triangular section of the liver and a gland at the hilus of the spleen and a left inguinal gland. The condition of the patient on leaving the table was very poor.

The histologic examination of the excised spleen revealed the splenic pulp to contain a multiplication of endothelial cells. The malpighian corpuscles were also hypertrophic, with obliteration of central arterioles. There were numerous large cells in alveolar arrangement. The connective tissues were increased slightly. Some of these groups of cells were intimately intermingled with blood corpuscles, showing occupation of the sinuses (fig. 5).

The roentgenogram [18] of the long bones taken on Feb. 25, 1927, showed definite bone changes in both femora and both tibiae (figs. 6 and 7). The femoral necks were markedly sclerosed, the angles were changed from the ordinary obtuse to right angles, and there was a pathologic fracture of the neck of the femur on the right side. The forming epiphyses for the upper ends of the femora were of normal size but a little irregular in outline. The joint spaces at the hips were normal. There was slight periosteal thickening and elevation on both sides of the femoral shafts in their middle halves.

The distal ends of the femora showed the changes that have been described as typical of Gaucher's disease, that is, a fulness of the shaft, particularly just above the medial condyle, causing an appearance that has been likened to an Erlenmeyer

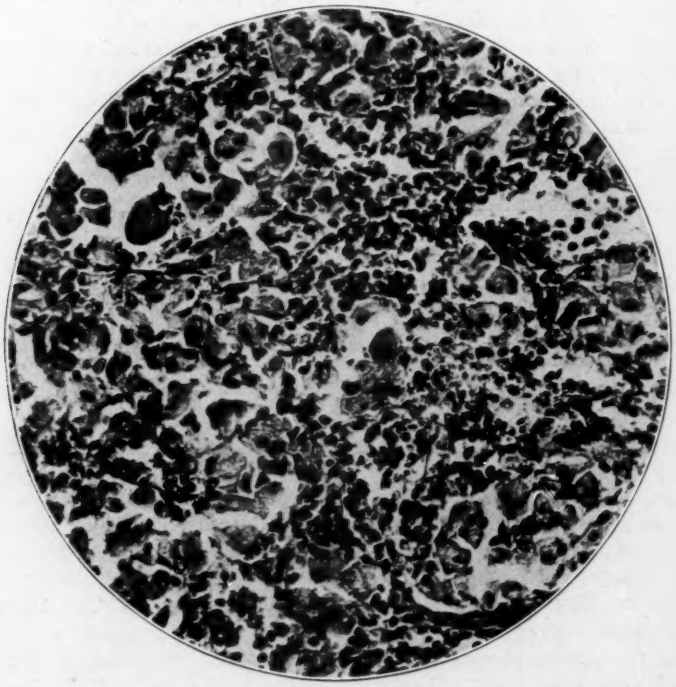

Fig. 5 (case 1).—Histology of the excised spleen, showing the alveolar arrangement of Gaucher cells in the splenic sinusoids.

flask. There was also flaring of the distal ends of both femora with faint growth arrest lines in the juxta-epiphyseal regions. In the lower one third of the femora where the fulness was most noted, the cortex was absent, and there were irregularly shaped areas of decreased density with an occasional area of sclerosis.

The tibiae definitely showed pathologic change, the cortex being very thin, with many patchy areas of decreased density scattered throughout the medullary portions, from just below the proximal epiphyseal lines to just above the ankles. There was also a general decalcification of the distal ends of the tibiae. The fibulae had in general the same changes observed in the tibiae, but were not so well visualized.

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18. The films were interpreted by Dr. Hillyer Rudisil, Jr., of the Department of Roentgenology, University of Chicago.

The changes described in the tibiae were even more striking in the humeri, with a loss of cortex in the upper thirds and a general decalcification giving the appearance of large cystic areas; the rest of the shaft on both humeri showed the small punched-out areas of decreased density described in the tibiae. Both radii and ulnae showed patchy decalcification in the proximal halves, but the distal portions were relatively normal. The elbow joints and wrist joints were normal (fig. 5).

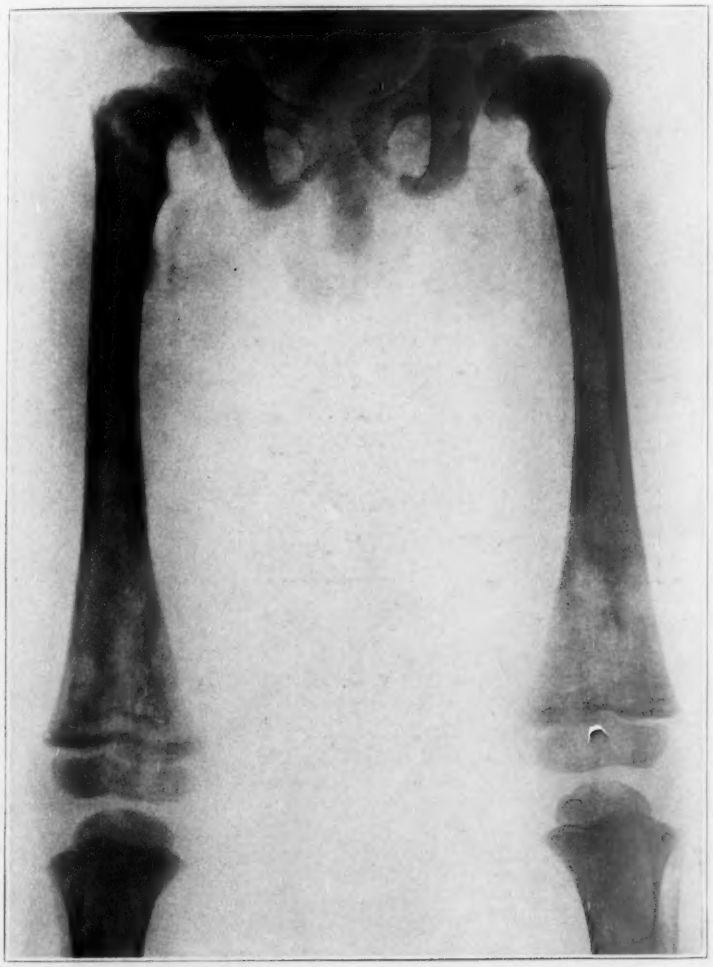

Fig. 6 (case 1).—Roentgenogram of both femora, including the hip joints, showing the typical changes described in the text.

The diagnostic impression was: (1) some general skeletal disease with a widespread involvement of the medullary portions of the long bones, suggesting a pathologic process of the bone marrow, and (2) changes in both femoral necks as already described, probably a part of the same process, but possibly caused by an entirely different process, such as rickets.

Following the operation, the patient's general condition slightly improved, and for two or three months after discharge, there was a fair degree of well-being. But gradually there appeared a strange train of symptoms which were referable to the central nervous system. For these and for a general check-up, the patient returned to the hospital clinic at various intervals. The more important findings as recorded in the chart may here be reproduced.

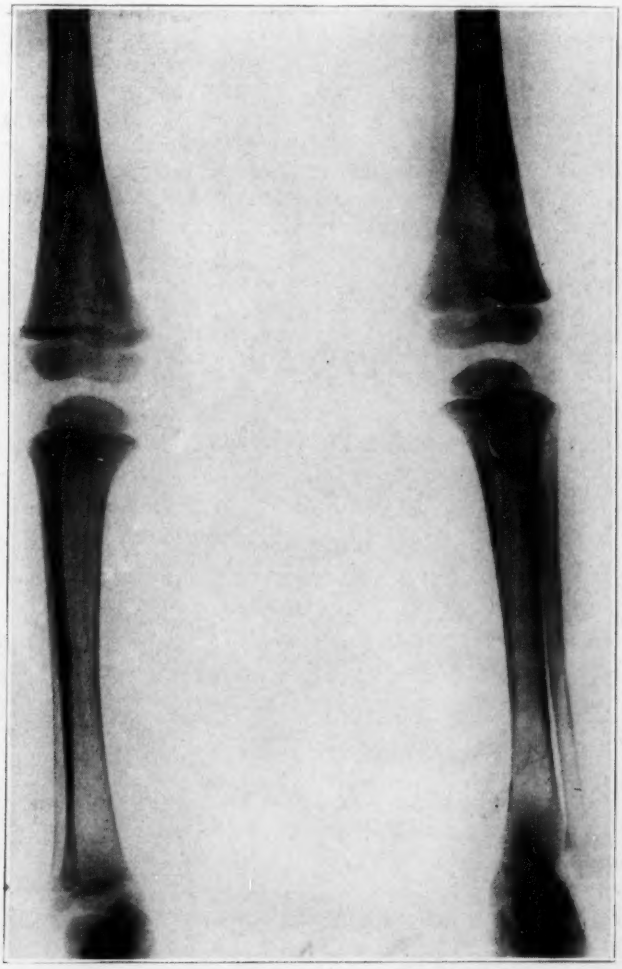

Fig. 7 (case 1).—Roentgenogram of the lower part of the legs, showing typical changes in the lower thirds of both femora and in both tibiae and fibulae.

May 13, 1926: The patient returned for a blood count, which showed: hemoglobin, 70 per cent (Tallqvist); red blood cells, 4,000,000, and white blood cells, 1,100, with a differential count of 65 per cent polymorphonuclear neutrophils, 25 per cent small lymphocytes, 5 per cent large lymphocytes, 1 per cent mononuclears, 2 per cent eosinophils and 2 per cent basophils. The patient had not had any nasal bleeding. She walked only with the aid of crutches.

Jan. 13, 1927: Physical examination showed all reflexes to be extremely exaggerated. The child appeared to be very nervous and the condition was almost that of tetany at the time of examination. There was a double Kernig sign which seemed to be very pronounced.

January 15: A neurologic examination revealed a slight paralysis of the left sixth cranial nerve. The pupils were apparently equal and reacted to light. There

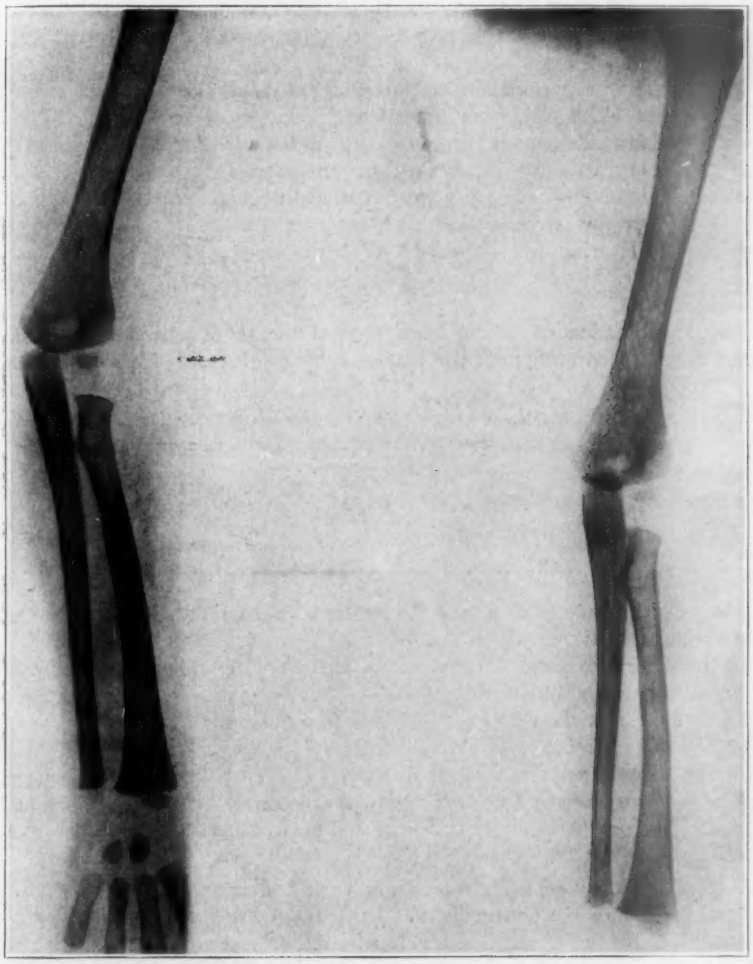

Fig. 8 (case 1).—Roentgenogram of the arms, showing typical rarefaction of the shaft and irregular outline of the cortex in the humeri, the radii and the ulnae.

were spastic reflexes in both arms and legs, with bilateral ankle clonus, but no Babinski sign. The patient was unable to walk. No nystagmus was noted. The fundi were pale, but the disks showed clear margins, and no hemorrhage, retinitis or venous stasis was noted. Sensation for pain was present.

January 16: The patient was seen to be in a contracted spastic condition, with spasmodic twitchings of the arms and legs. Both eyelids were edematous and

draining, with evidence of conjunctival inflammation. The pupils reacted to light. The neck was stiff and painful on motion. There was slight lymphadenopathy. All muscle reflexes were increased, but no Babinski or Oppenheim sign could be elicited.

January 17: There was a moderate amount of nasal bleeding. The Kernig sign was positive. Examination of the blood at this time showed: hemoglobin, 85 per cent (Tallqvist); red blood cells, 3,045,000, and white blood cells, 24,200, with a differential count of 56 per cent polymorphonuclear neutrophils, 13 per cent small and 13 per cent large lymphocytes, 16 per cent mononuclears and 2 per cent basophils.

Dr. Meyers, in a consultation on March 11, noted that the neurologic symptoms were due to a blood clot, from brain hemorrhage, in the cerebrum. Spasticity seemed to be increasing, as it was generalized in both arms and legs, with positive ankle clonus but a negative Babinski sign. Sensation was apparently preserved. No nystagmus and no ocular palsy were seen, and the optic nerve showed no choking, as the margins were distinct, although the disks were pale and partially degenerated. Hearing was impaired. With the history of repeated generalized convulsions, Dr. Meyers made the diagnosis of hemorrhagic encephalitis as a probable lesion.

Chemical examination of the blood showed the results given in table 2, all figures expressed in milligrams per hunded cubic centimeters of blood.

TABLE 2.—*Chemistry of the Blood in Case 1*

Date	Calcium	Phosphorus	Sugar	Total Nonprotein Nitrogen	Creatinine Preformed	Uric Acid
2/21/27	11.2	...	...	..	...	...
2/28/27	11.3	4.5	125	30	1.3	2.8

The patient steadily failed, and the nervous manifestations continued to grow more serious. In the spring of the following year, she was totally unable to eat her food by her own effort. Her power of vision progressively diminished, so that she could not clearly discern the objects in her immediate surroundings. She was in a constant spastic state, her upper and lower extremities showing tonic and clonic contractions more or less continuously during the waking hours. When she fell asleep, these spastic movements disappeared. There was occasional edema of the face and extremities. During the presence of edema, the spasticity became less noticeable. She became greatly emaciated and finally died on April 12, 1928, at the age of 7 years.

CASE 2.—*History.*—Y. W. was a full term and normally delivered boy, the younger brother of the patient in case 1. He had trouble with his vision early, especially in focusing on an object, primarily due to converging strabismus. At 2 years of age, he fell and sustained a slight fracture of the iliac bone, for which a physician applied a plaster of paris cast for four weeks. After this he was able to walk for a while, but his enlarging abdomen caused much discomfort. In December, 1925, when the patient was 3 years old, the abdomen became very large, and at the time of his admission to the Los Angeles General Hospital on Jan. 15, 1927, he was practically unable to walk.

Examination.—Physical examination at this time revealed a well nourished boy, sitting up in bed, apparently not acutely ill. The scalp was very dry and scaly. The external auditory canals were inflamed, and both drum membranes appeared slightly dull. The eyelids were slightly edematous. Both pupils were equal and reacted

to light and in accommodation. Slight weakness of the left sixth nerve was observed. The fundi were normal. No icterus was present. There was a moderate amount of nasal discharge. The pharynx was slightly inflamed and the tonsils hypertrophied. The neck was not rigid, and slight bilateral adenopathy was present. Respirations were 24 per minute, and coarse breathing over both apexes was noted anteriorly and posteriorly. No areas of dulness or râles were present. The heart sounds were normal and the borders within the normal limits. The pulse was regular, and the rate was 110 per minute.

The abdomen was markedly distended and tense. There was no ascites. The spleen filled the entire left side of the abdomen almost to the groin and extended to the median line. The liver was slightly enlarged. The genitalia were normal. A generalized spasticity of musculature was noted. The reflexes were extremely exaggerated, with a tendency to a Kernig sign and ankle clonus. There were brown spots over the entire body. The child's weight was 34 pounds and 7 ounces (15.6 Kg.).

Course.—The day after admission, the child's temperature rose to 103.2 F., and he had a profuse nosebleed, which was controlled by packing the left nostril and injecting 5 cc. of thromboplastin. Later the same day, nosebleed again resulted

TABLE 3.—*Condition of the Blood in Case 2*

				Differential Count, per Cent						
					Lymphocytes					
Date	Hemoglobin (Tallqvist), per Cent	Red Blood Cells in Millions	White Blood Cells in Thousands	Polymorphonuclear Neutrophils	Small	Large	Mononuclears	Basophils	Eosinophils	Platelets
1/15/27	70	3.850	6.90	73	23	4	..	..	..	.....
2/ 3/27	..	.....	.....	44	35	10	10	1	..	40,000
6/26/30	68	3.150	12.55	47	48		3	1	1	157,000

when a swab was taken for culture. On the following day, the temperature fell to normal. There were no further nosebleeds. The Mantoux reaction was negative. No pathologic process was present in the chest. On January 20, a note was made that the child perspired profusely while sleeping. On January 26, examination by the neurologic department revealed no evidence of nervous pathologic involvement. There was no further rise in temperature, and on February 4, splenectomy was performed, from which the child made an uneventful recovery. On March 7, the generalized muscular spasticity was again present, and a convergent strabismus was noted.

Urinalysis showed an acid reaction, a specific gravity of 1.025, with a few granular casts, but no albumin and no sugar.

The fragility test showed initial hemolysis at 0.48 per cent and complete hemolysis at 0.36 per cent.

Results of the blood examinations are given in table 3.

The roentgenograms of the long bones, made on February 24 and 25, revealed some general rarefaction of these bones. The epiphyses appeared normal, except that the upper epiphyses of both femora showed gross irregularity of the epiphyseal lines, associated with coxa vara, giving the appearance of a gross disturbance of growth at these points.

Splenectomy was performed by Dr. C. T. Sturgeon on February 4. He found that the spleen was greatly enlarged, extending from the diaphragm down to below the crest of the ilium. There were a few adhesions posterior to the abdominal wall. The liver was also enlarged, extending about three fingerbreadths below the costal

arch. The gallbladder was visualized but appeared to be normal. No other pathologic change was searched for. No abdominal fluid was present.

The pathologic report on the excised spleen was as follows: The specimen consisted of a spleen that weighed 550 Gm. It was greatly enlarged, the greatest dimensions being 20 by 12 by 5 cm. On one edge it presented two deep notches and on the opposite edge two shallow ones. The capsule was smooth and thin throughout, and pale grayish red. The consistency was slightly increased, and on section, the surface had no resemblance whatever to normal splenic parenchyma, but was of a uniform grayish-red color which was finely granular, with occasional small hemorrhagic spots. There was slight eversion of the cut edge.

Microscopic examination of the spleen showed very little normal architecture of the spleen, with marked hyperplasia of the sinus endothelium. The presence of large cells in great number was very similar to that found in the spleen of the patient's sister. A diagnosis of Gaucher's disease was made.

After the operation the spasticity of the extremities gradually grew worse, with constant tonic and clonic contractions of the muscles in these regions. The eye defect which was an early complaint also became worse, the patient failing to notice objects properly. The reflexes became greatly exaggerated.

On June 26, 1930, examination of the blood revealed practically no change. The bleeding time was one minute, and the coagulation time two minutes. The reticulocytes were 1.5 per cent of the total erythrocytes. The indirect van den Bergh test showed the bilirubin equal to 0.71 units, or 3.55 mg. per hundred cubic centimeters of serum, while in the direct test the color began to develop in one and three-quarter minutes and reached the maximum in thirty-five minutes (delayed reaction). The Wassermann and Kahn reactions of the blood were negative.

The condition of the patient grew continuously worse, and he finally died at the age of 6 years, with all the symptoms that characterized the last days of his elder sister.

Case 3.—*History.*—Y. W., the youngest member of the same family, was first seen when the child was 15 months of age, the complaint being gradually increasing size of the abdomen and inability to gain weight. The birth history was normal in every way, and the child was still being nursed by the mother at the time of the first examination. The child was very undernourished, weighing only about 16 pounds (7 Kg.), and had a dry, pale skin and poor tissue turgor. The abdomen was protuberant, and the splenic edge was palpable at about one fingerbreadth below the costal margin. The liver appeared to be enlarged also, its edge being felt about the same distance below the right costal arch. The superficial veins over the anterior surface of the trunk were prominent. No other definite findings were noted. The usual laboratory tests and roentgenographic examinations of the skeletal system did not yield any additional pathologic process. The blood count made on June 5, 1930, showed: hemoglobin, 65 per cent (Tallqvist); red blood cells, 3,150,000, and white blood cells, 8,200, with a differential count of 78 per cent total lymphocytes, 12 per cent polymorphonuclear neutrophils, 8 per cent monocytes, 1 per cent eosinophils and 1 per cent basophils. On the basis of the course and outcome of the cases of the two older members of the family, a tentative diagnosis of Gaucher's disease was made, and hospitalization was advised.

Course.—On account of the unsatisfactory results, however, in the case of the other two children, the parents refused to place the child in the hospital. The treatment consisted of dietary supervision and weekly intraperitoneal injections of the whole blood obtained from either parent. The mother stated that the child's general condition seemed to improve after the injections of blood. After about five months of treatment, the child died of bronchopneumonia at the age of 2 years.

AN IMPROVED PROTECTIVE DEVICE IN THE TREATMENT OF INFANTILE ECZEMA*

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AND
GOLDIE MAHAN KEITH, R.N.
CINCINNATI

The necessity of protecting the face of babies suffering from infantile eczema, with its attendant distressing symptom of itching, frequently taxes the ingenuity of both nurses and doctors.

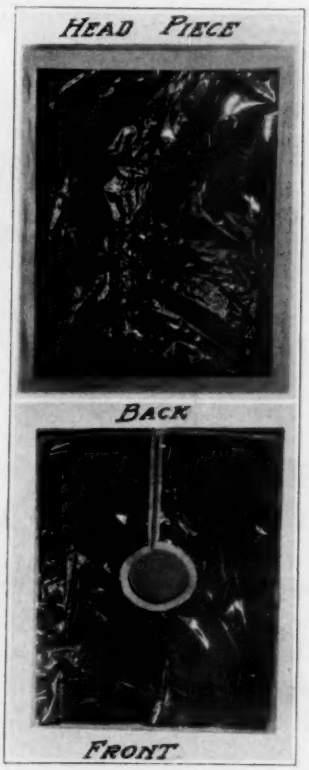

Fig. 1.—Head piece and shoulder piece ready for adjustment.

The following device was constructed by one of us (Mrs. Keith), and was found to be of definite value. As can be seen from the

* Submitted for publication, May 19, 1931.

* From the Pediatric Department of the Jewish Hospital.

accompanying photographs, it consists of two pieces of cellophane, one piece 16 by 20 inches (40.64 by 50.80 cm.), which is fastened on the bed by adhesive strips, the other piece 14 (35.48 cm.) by 16 inches, (the size varies according to the size of the patient), with an area 3½ inches (9 cm.) in diameter cut from the center, with an opening extending from this circle to the edge of the cellophane. All of the edges are bound with adhesive plaster, ½ inch (1.27 cm.) wide, and the circle in the center is covered by overlapping pieces of adhesive plaster from ½ to 1 inch (2.5 cm.).

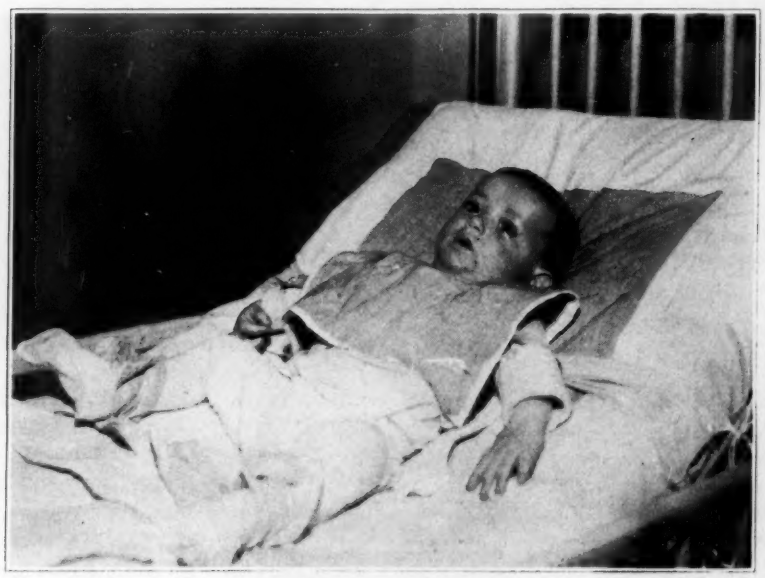

Fig. 2.—Appearance of device in place.

When completed, the jacket is placed on the child, and the edges are brought together in the back and fastened with adhesive plaster. The lower edges are brought together under the arms and fastened together with safety pins, pinned into the binding. The child is then laid on the bed, so that the head rests on the cellophane, which is fastened to the sheets. The arms and legs are restrained, and in this position the baby may strain and rub its face without injuring the eczematous areas, because the smooth cellophane covering offers no resistance.

This device is simple and inexpensive, and lasts for twenty-four hours.

Case Reports

PSEUDO-APLASTIC ANEMIA*

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The confused state of the idiopathic anemias, so far as the classification and nomenclature are concerned, has become more evident since the modern methods of investigation were disclosed. The regrouping of those cases which were previously included under von Jaksch's and Banti's anemia have clarified the situation to some degree. The true picture of aplastic anemia as is held by most clinicians consists of a severe anemia which develops rapidly over a period of from six weeks to four months ending fatally within six months or less. The other formed elements of the blood stream, the leukocytes and the platelets, show a similar numerical reduction. Associated with this, according to Lucas, there may or may not be an increase in the lymphoid structures, the lymph glands, the spleen and the liver. The postmortem finding of a marrow with the active elements replaced by fatty tissue has been included as the characteristic feature of this disease. The following case gave evidence during life of all the features of aplastic anemia, but at autopsy gave evidence of an actual hyperplasia of the hematopoietic structures. It is for this reason that the necessity for the term pseudo-aplastic anemia presented itself.

REPORT OF CASE

History.—J. D., aged 3 years, was admitted to the pediatric service of the Coney Island Hospital on Aug. 4, 1930, with a history since June, 1930, of increasing pallor, weakness and a distended abdomen. Intermittent attacks of colic and diarrhea occurred, lasting about from three to seven days, during which time the pallor increased, the patient lost weight, and the abdomen was observed to enlarge. During the free periods, the abdomen became smaller, and the patient improved in strength and regained some of her color, but each time her condition was worse than in the preceding free period.

The family history was essentially negative. One brother was alive and well. The father and mother were alive and well. The important features of the patient's past history were chickenpox when 2 years old, pertussis when 8 months old, frequent colds, and the mother's statement that the patient was nearly always in poor health and did not seem to thrive and develop as well as her brother.

* Submitted for publication, April 20, 1931.

Physical Examination.—Physical examination on admission revealed a markedly pale, white, female child who appeared fairly well nourished. The abdomen was very prominent. The skin had a waxy appearance with a yellow lemon-colored tint. The ears were normal. The eyes reacted to light and accommodation. The mucous membrane showed extreme pallor. The pulmonary fields were normal. The heart was moderately enlarged. The heart sounds were regular and of a fair quality. The second pulmonic sound was accentuated. There was a faint systolic murmur, with greatest intensity in the apical region. The lymph glands in the cervical, axillary and inguinal regions were enlarged, ranging in size from that of a small pea to that of a small bean. The abdomen was distended. The liver was enlarged; the edge was firm and palpated at the level of the umbilicus. The spleen was firm and extended out to the midline and about 1 inch (2.5 cm.) below

Appearance of the patient.

the umbilicus. The abnormalities observed in the bones were prominent frontal bosses and slight beading of the ribs. The deep and superficial reflexes were normal. Roentgen study of the long bones and the bones of the skull revealed no evidences of rickets or syphilis. At the lower ends of the diaphysis of the radii, femora and tibia, slight thickening of the trabeculae was observed. The roentgen shadow of the heart showed enlargement both to the right and to the left.

Laboratory Data.—The stools did not contain ova; the predominating organism was *B. coli.* Urinalysis gave negative results on August 8 and 23.

The Mantoux test gave positive reaction to 0.1 mg. of tuberculin.

Cultures from the nose and throat were negative for the Klebs-Löffler bacillus.

Vaginal smears were negative for gonococcus.

Examination of the Blood.—Chemical analysis showed: calcium, 11.5 mg.; phosphorus, 2.7 mg. (normal from 3.3 to 6.6 mg.); icteric index, 3.5; van den Bergh test, direct and indirect, negative; fragility test, 0.42, beginning of hemolysis,

and 0.32, complete hemolysis; bleeding and coagulation time, normal; Wassermann reaction of patient, mother and father, negative (type II Jansky).

The blood counts are given in the accompanying table.

Treatment and Course.—Therapeutic measures were directed mainly against the extreme anemic condition. Direct transfusions of 200 cc. of blood were given on August 8 and 18 and October 10 and 29. Bone marrow, liver, iron products and ultraviolet ray treatment were also given.

While the patient was in the hospital, the course of the illness was observed to be definitely downhill, with little or no response to treatment. After the second transfusion, there seemed to be slight improvement, and on September 9 she was released from the hospital on signature of the parents. Two weeks later, the patient was examined at home during one of her previously described attacks of colic. The temperature was 103 F., and there were extreme pallor and considerable

Blood Counts

Date	Red Blood Cells	Hemoglobin, Index	Per Cent	White Blood Cells	Basophils	Eosinophils	Myelocytes	Juvenile Cells	Stab Cells	Segmented Polymorphonuclears	Lymphocytes	Mononuclears	Nucleated Red Cells
Aug. 4.....	2,150,000	35	0.81	2,500	..	..	2	2	3	28	57	8	5
Aug. 8, one hour after transfusion	.....	..	....	.....	..	..	..	..	..	17	68	7	..
Aug. 8, seven hours later	.....	..	....	.....	..	1	4	5	3	17	67	3	..
Aug. 20.....	2,000,000	45	1.0	3,600	..	..	1	1	2	19	75	2	..
Aug. 26, second transfusion	2,000,000	50	1.2	2,000	..	1	1	1	3	18	74	2	..
Sept. 1.....	2,100,000	45	1.1	4,000	..	3	3	3	7	29	54	..	..
Sept. 9.....	.....	50	....	.....	..	..	4	3	1	23	64	5	..
Oct. 8.....	.....	..	....	.....	2	1	2	1	4	35	50	5	7
Oct. 27.....	1,560,000	40	1.3	2,200	..	..	4	4	2	18	68	4	1
	Platelets												
Aug. 6.....	63,000												
Aug. 28.....	120,000												
Oct. 11.....	77,000												
Oct. 16.....	65,000												

tenderness in the left hypochondrium. The hemoglobin determination at this time was 40 per cent, with practically no change in the differential count. Observation two days later revealed further enlargement of the spleen, which extended well below the umbilicus. There was no rise in temperature, and the splenic tenderness and pain had disappeared. On October 7, the hemoglobin determination was 27 per cent, and readmission to the hospital was advised.

Transfusions were given. Examination of records of the blood count before and after the transfusions indicated their futility. One, two, eight, twenty-four and forty-eight hour determinations of the hemoglobin and red blood cells indicated that the injected blood disappeared from the circulation almost immediately. There was a slight general reaction to the first three transfusions, but after the last transfusion, the reaction was so great that it apparently overwhelmed the patient, causing death. Reactions of this type to blood transfusions in patients with blood dyscrasias are common for some unexplained reason.

Autopsy.—Autopsy was performed by Dr. D. Groszberg, and he reported as follows: The body was that of a poorly developed and emaciated white female

child. The skin throughout the whole body had a distinct yellowish pallor. The incision was made from the larynx to the symphysis.

Thymus: The thymus was rather small, weighing 6.5 Gm. It was rather firm, and on cross-section it appeared grayish yellow.

Thyroid: The thyroid showed the usual three-lobe structure; it weighed 5 Gm. On cross-section, it was red.

Lungs: Both lungs were free and pink, and on touching, they crepitated. On both lower lobes posteriorly, under the visceral pleura, there was a small, firm, white nodule that gritted on the knife (it was apparently calcified). The lobes were about 3 mm. in diameter. On cross-section, the lungs showed the usual structure. The mucosa of the larynx, trachea and bronchi was pale.

Heart: The heart was considerably enlarged. The parietal pericardium was adherent to the visceral pericardium practically over the entire surface. The adhesions were firm and broke with difficulty, revealing numerous pockets, in which about 100 cc. of serosanguineous fluid was encapsulated. The heart muscle was pale pink. The left ventricle showed considerable hypertrophy. The thickness of the wall was about five eighths of an inch (0.9 cm.). The mitral valves were thickened. The anterior flap showed considerable thickening. The posterior flap was adherent to the ventricular wall. There was some thickening of the tricuspid leaflets. The aortic and pulmonic cusps were thin, translucent and glistening.

Spleen: The spleen was adherent to the surrounding structures by flat, thin adhesions that could be broken with little difficulty. The dimensions of the spleen were as follows: length, 22 cm.; width, 11 cm., and thickness, varying from 2.5 cm. to 7.5 cm. The weight was 800 Gm. The capsule was covered partly by remnants of the connective tissue adhesions and partly by milky, irregular patches.

In the hilus there were two round, nodular structures, 20 and 25 mm. in diameter, respectively. On cross-section, these nodules had the structure of the spleen. The cut surface was smooth and dark red. The follicles and trabeculae were well visualized. The pulp scraped off quite easily.

Liver: The dimensions of the liver were 20 by 20 cm., and it weighed 1,240 Gm. Glisson's capsule was thin, smooth and translucent. The surface was mottled due to brownish-red and yellow areas that were intimately intermingled. On cross-section, the surface had a yellowish hue, in addition to the brown color.

Gallbladder: The gallbladder was of the usual shape and size. The wall was thin and contained dark green, viscous bile.

Kidneys: The kidneys were of the usual shape and size; they were pale. The capsules stripped easily, leaving smooth surfaces. On cross-section, the structure was well maintained.

Suprarenals: The suprarenal glands had the usual yellowish color and were triangular. Cut sections showed the yellow cortex and red medulla in the usual proportions.

Gastro-Intestinal Tract: The esophagus was of normal size and shape; its mucosa was pale. The mucosa of the stomach was pale. The ileum and jejunum showed hypertrophy of Peyer's patches, which had a pinkish, irregular, raised, lobulated surface. The wall of the large intestine was thickened to three times its normal thickness. The mucosa was studded with numerous small, purplish, raised, nodular areas, which on cross-section gave the appearance of lymphoid tissue.

Lymph Glands: The lymph glands were enlarged, varying in size from that of a pea to that of a lima bean in the mediastinum, mesentery, retroperitoneal,

axillary and inguinal regions. On cross-section, these glands were reddish pink. The surface bulged out considerably.

Genitalia: The uterus, tubes and ovaries corresponded to the age and development of the body.

Bone: The bone marrow of the right femur, including the head and part of the shaft and that of the eleventh and twelfth thoracic and first lumbar vertebrae, ribs and clavicle, was dark red and jelly-like.

Microscopic Observations.—Microscopic study of all of the organs showed the usual structures in normal proportions, except in the spleen, liver and lymph glands. The spleen showed a large number of cells. These cells were mostly of the mononuclear lymphocytic type. Intermingled with these were groups of red blood cells, some nucleated, some nonnucleated and others disintegrating. There were also numerous granular immature cells. The interstitial connective tissue and the reticular tissue were increased.

The liver cells had a normal appearance. The interstitial connective tissue was slightly increased.

The lymph glands showed the usual structure, except for a moderate increase in interstitial tissue and cellular elements.

The bone marrow showed an increase of the usual cellular elements.

The pathologic diagnosis was: adhesive pericarditis with effusion; endocarditis; mitral valvular disease; splenomegaly; perisplenitis; hypertrophy of the liver; hypertrophy of all the lymph glands and lymphatic structures of the intestines; hypertrophy and hyperplasia of the bone marrow; calcified Ghon's nodules in both lungs.

COMMENT

In a discussion of the differential diagnosis, any condition in which an enlargement of the spleen, liver and lymph nodes occurs, those in which, in addition, pericarditis, endocarditis, a positive Mantoux test and evidences of healed tuberculous lesions occur and, lastly, those in which aplastic blood pictures occur must be considered and ruled on.

During the entire course of the patient's illness, the working diagnosis was primary aplastic anemia. In view of the rapid downhill course and the extreme reduction of all the formed elements in the blood, this opinion seemed warranted. Against this diagnosis was the absence of a tendency toward hemorrhages from the mucous membranes. Final exclusion of the diagnosis was established by the finding of the hyperplastic bone marrow. It is conceivable that there may be a hypofunction coexistent with a hyperplasia as a result of the failure of the normal method of regulation of hematopoiesis. Hematologists vary in their opinions as to the source of this regulation. Some of their theories are as follows:

1. Hormones in varying amounts that are normally in the circulation regulate the hematopoietic tissue.

2. Regulation of hematopoiesis is controlled by the vegetative nervous system.

3. Regulation of hematopoiesis is through an internal secretion from the spleen.

4. The by-products of destroyed and disintegrating blood cells regulate the hematopoietic organs.

Actual proof for any of these theories is still lacking. In my case, there was no evidence of overdestruction or underproduction of the formed blood elements, still a typical aplastic picture was observed clinically. The inhibitory influence that prevented the blood cells from entering the circulation was not determined.

Pernicious anemia was considered because of the lemon-yellow color of the skin, the extreme anemia, the presence of a hemoglobin index of more than 1 in the examinations of the blood on August 26 and September 1 and the red jelly-like bone marrow found at autopsy. The general opinion of hematologists is that pernicious anemia does not occur in childhood. Further facts against this diagnosis in the case reported were the absence of neurologic features, digestive disturbances and macrocytosis. In addition, it may be added that the enlargement of the spleen and liver reached in my case does not occur in this condition.

Cooley's erythroblastic anemia was ruled out by the absence of large numbers of erythroblasts in the blood, and the absence of the characteristic widening of the medullary portion, thinning of the cortex and thickening of the trabeculations of the flat and the long bones. Cooley also indicated that these cases usually occur in infants and children who are descendents of, or resident natives of, the countries surrounding the Mediterranean Sea. The parents of my patient were American born and of English derivation.

Banti's disease was excluded because of the absence of advanced cirrhosis of the liver and its accompanying ascites, varices of the esophageal veins and hematemesis usually found in this symptom complex. This disease occurs mostly in young adults.

Gaucher's disease was not seriously considered because of its extreme rarity, and was ruled out finally after autopsy by the absence of the large, pale, granular, vacuolated cells in the spleen and other organs.

Niemann-Pick's disease is characterized by a similar enlargement of the spleen, liver and lymph nodes, in which are found cells the cytoplasm of which is replaced by a lipoid substance that gives the cells a foamy appearance; there is also an increase of cholesterol in the blood. These features were not present in my case.

Hodgkin's disease was not considered owing to the absence of a great enlargement of the lymph glands.

A picture of aplastic anemia is observed in poisoning by the x-rays, radium, gas, benzene and phenylhydrazine, and also in *Bothriocephalus latus* infection. Careful inquiry into the history of the patient and an investigation of the stools ante mortem and the intestines post mortem excluded this possibility.

In congenital syphilis, the spleen and liver do not reach the proportions found in the case reported. The Wassermann report was negative on the blood of the patient, her parents and a brother.

Of the three types of leukemia, lymphatic, myelogenous and aleukemic, the aleukemic was considered as a great likelihood. The presence of leukopenia through the entire course of the illness, as in the case reported, has been observed in other recorded cases. In this condition, the other formed elements of the blood are also reduced considerably. The great enlargement of the liver and spleen found in my case is characteristic of the leukemias. The postmortem findings, in addition to this condition of the spleen and liver, hyperplasia of all the lymph glands, Peyer's patches and bone marrow, favored this diagnosis. The absence of transient rises in the leukocyte count and spontaneous hemorrhages were the only clinical features that failed to complete the picture. The blood smear examinations failed to aid in identifying the type of leukemia present. There was not a sufficient predominance of lymphocytes to classify it as a lymphocytic leukemia, nor was there a sufficient predominance of immature granular cells to classify it as a myelogenous leukemia. This fact also restrained me and my associates from finally considering the case as one of aleukemic leukemia.

Another condition that was brought into discussion after autopsy was congestive cirrhosis of the liver, or its more advanced condition, which is commonly known as Pick's disease. This is characterized by evidences of tuberculous infection, enlargement of the liver and spleen and generalized serositis involving the pleura, pericardium, endocardium, peritoneum and synovial membranes. In the case reported, there were evidences of healed pulmonary infection in the form of calcified subpleural Gohn's nodules in both lower lobes, a positive Mantoux test, enlargement of the liver and spleen with moderate cirrhosis, a marked pericarditis and a mild endocarditis.

The foregoing discussion brings out the difficulties encountered in the differentiation of splenic anemias. One cannot help feel that there may be a common etiologic basis in most of the conditions that are now classified as separate entities on minor characteristics.

In reviewing the aforementioned possibilities, the conditions with which the case under consideration seems to have more signs in common are aplastic anemia, but not in pure form in view of the postmortem findings in the bone marrow, aleukemic leukemia and congestive cirrhosis of the liver.

The diagnosis that seems to cover the clinical and postmortem findings best is pseudo-aplastic anemia associated with a leukemic pathologic picture. Congestive cirrhosis of the liver cannot be ruled out entirely.

MULTIPLE TUBERCULOUS LESIONS IN THE BRAIN OF A CHILD (TUBERCULOUS ENCEPHALITIS) *

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Tuberculous lesions in the brain are not uncommon in children. Such lesions usually occur singly. Friedenwald and Greenfeld,[1] however, reviewed the literature and cited several instances of multiple tuberculous lesions. Their own patient, a Negro boy of 7 with generalized tuberculosis, had five lesions, from 0.75 cm. to 2 cm. in diameter, at various locations in the cerebral hemispheres, and a very early meningeal involvement. Death occurred seven months after the first of a series of epileptiform seizures. Other instances of multiple lesions have been reported by Thiele[2] (five lesions), Dalton[3] (three lesions), Stevens[4] (from six to eight lesions), Sachs,[5] Combe[6] and Ewald.[7] In some instances there were localizing symptoms; in others, none. In Sach's patient, there was extensive degeneration of the fiber tracts of the spinal cord.

The following case is unusual because of the large number of brain lesions without localizing signs or symptoms.

REPORT OF A CASE

History.—A Negro girl, aged 4 years, first came under observation at the Evanston Hospital clinic because of poor appetite, a fever that had appeared every

* Submitted for publication, May 7, 1931.
* From the Children's Memorial Hospital, Chicago, and the Otho S. A. Sprague Memorial Institute.

1. Friedenwald, Edgar B., and Greenfeld, W.: Tuberculous Tumors of the Brain, Am. J. Dis. Child. **9**:508 (June) 1915.

2. Thiele, F.: A Case of Cerebral and Cerebellar Tumors with Well Defined Tract Degenerations, Brain **24**:509, 1901.

3. Dalton, Norman: Multiple Tubercular Tumors of the Brain in a Child Age 1 Year, Tr. Path. Soc. London **40**:20, 1899.

4. Stevens, J. L.: Multiple Tubercles in the Brain, Glasgow M. J. **38**:149, 1890.

5. Sachs, B.: Diseases of the Mid Brain Region, Am. J. M. Sc. **101**:233 (March) 1891.

6. Combe: Rev. méd. de la Suisse Rom. **12**:686, 1892, quoted by Friedenwald and Greenfeld (footnote 1).

7. Ewald: Berl. klin. Wchnschr. **28**:261, 1891, quoted by Friedenwald and Greenfeld (footnote 1).

evening for more than a month and an infection of the foot. She was found to have an infection of the upper respiratory tract and a draining sinus on the outer aspect of the third right toe adjacent to the next toe. The etiology of this infection was unknown, but it may have been caused by the nail of the next toe. Wet dressings were advised.

About two weeks later, she had a convulsion, and was again seen at the Evanston Hospital (by Dr. Robert Blessing). At that time she had a marked trismus, fixed contracted pupils and an absence of all reflexes. She was thought to be suffering from tetanus and was referred to the Children's Memorial Hospital.

At the latter institution additional pertinent facts regarding the child were revealed. For five months she had had little appetite, had lost weight and had been drowsy. During that time her disposition had gradually changed. The lesion on the right foot already described had started as a blister which ruptured and discharged, and had persisted for two months. For two months she had had a fever nearly every evening. On the day of the convulsion, she was unconscious for a short time before and after the convulsion.

The child had had varicella in infancy, pertussis at 2 years and measles at 3.

A paternal aunt who was suffering from tuberculosis visited the child occasionally. Another paternal aunt had died of tuberculosis. There was one other child in the family alive and well.

Examination.—The child was restless and semicomatose. The pupils were dilated, but equal and regular. The entire pharynx was hyperemic. Respirations were slow and deep. The pulmonary fields were resonant throughout, but many fine râles were heard over the lower portions of the lungs posteriorly. The abdomen was level, and no viscera were palpable beyond normal limits. There was some rigidity of the neck and a suggestion of a positive Brudzinski sign. The spinal fluid pressure was increased; the cells numbered 120 per cubic millimeter, of which 81 per cent were lymphocytes; the Pandy test was positive; the sugar was 38 mg. per hundred cubic centimeters; the Wassermann reaction was negative, and the smear showed no organisms. The hemoglobin was 75 per cent (Dare), the erythrocytes numbered 4,160,000 and the white blood cells, 10,000 per cubic millimeter, of which 65 per cent were polymorphonuclears. The intradermal tuberculin test was positive.

A roentgenogram of the chest showed fine stippling over both lung fields.

The clinical diagnosis was tuberculous leptomeningitis with miliary tuberculosis of the lungs.

Course.—The course of the disease in the hospital was marked by a progressive but variable coma and neurologic signs that varied from day to day. Frequent spinal taps were made, which occasionally lessened the depth of the coma. The meningeal signs became more prominent. At times respirations were of the Biot type. The signs in the chest remained quite constant. There was a gradual increase in the cells and a decrease in the sugar of the spinal fluid, as is shown in the following tabulation:

Date	Cells per C. Mm.	Lympho-cytes, %	Mg. of Sugar per 100 Cc.
4/21/30	120	81	38 (admission)
4/28/30	400	100	26
5/8/30	690	100	
5/14/30	980	100	22
5/19/30	1,730	100	

Death occurred one month after entrance to the hospital and six months after the onset of symptoms.

Necropsy.—The body was moderately emaciated. The head was symmetrical, but fairly large. The right pupil was larger than the left. The chest was long and narrow, and the abdomen was scaphoid. There were no palpable lymph nodes.

Over the inferior surface of the brain, from the optic chiasm to the midportion of the medulla, the pia was thickened and infiltrated with fibrin. On the inferior surface of the temporal lobes and along the course of the middle cerebral vessels were numerous pinpoint to slightly larger gray tubercles in the substance of the

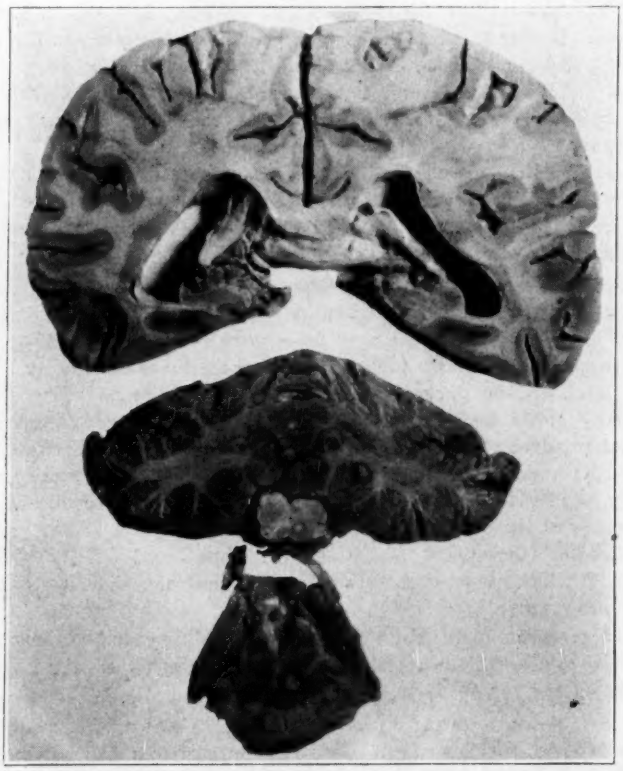

Fig. 1.—Frontal sections through various portions of the brain showing general distribution and relative number of lesions.

pia. Over the upper surface of each occipital lobe was a mass of confluent tubercles in the pia and brain substance. These masses measured 1 by 0.5 cm. The vessels of the pia were greatly engorged.

Scattered throughout the brain were 100 or more gray-green, spherical lesions, which varied in size from that of a pinhead to that of a pea (fig. 1). These were found in the cortex, subcortical region, white matter, basal nuclei, pons, medulla and cerebellum. In the right occipital lobe there was a yellow-gray, triangular area of softening surrounding one of the sulci. All of the lesions of the brain were encircled by a halo of hyperemia. The cerebral ventricles were greatly dis-

tended and each foramen of Monro measured 5 mm. in diameter. There were numerous fibrinous adhesions about the recesses of the fourth ventricle.

The thymus weighed 6 Gm. There was no effusion about either lung. Over the posterior surface of each lung were fibrinous pleural adhesions. Scattered throughout both lungs were numerous miliary tubercles. The lungs were otherwise crepitant. The bronchial mucosa was diffusely hyperemic. Between the two main bronchi were several slightly caseated lymph nodes, varying in size from that of a pea to that of a bean.

The spleen was large, soft and adherent to the diaphragm. The malphigian corpuscles were large and numerous, but no tubercles could be detected.

There were numerous miliary tubercles in the kidneys and diaphragmatic peritoneum. The other viscera were grossly normal. The lungs contained scattered

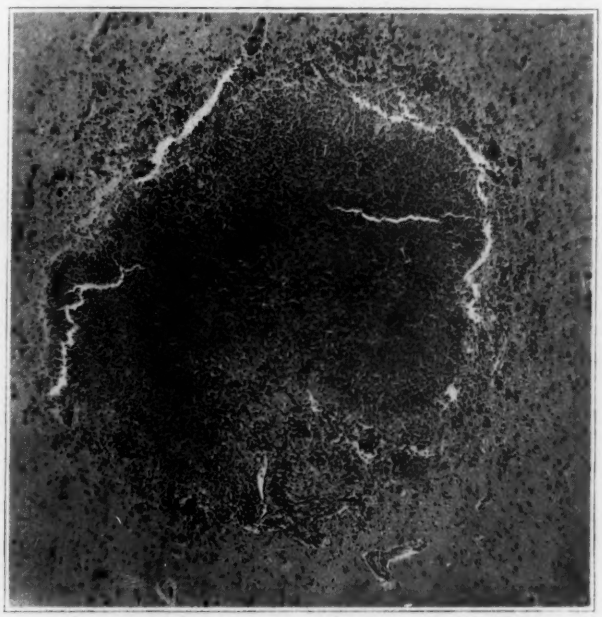

Fig. 2.—A typical lesion in the cerebral cortex.

miliary tubercles and a rather diffuse inflammatory process. Miliary tubercles were also present in the liver, spleen and kidneys.

Scattered throughout the brain were masses of caseated material surrounded by epithelioid and lymphoid cells and a few polygonal cells, with small, dense, eccentric nuclei. No giant cells typical of tuberculosis were seen, but there were a few cells resembling the foreign body type of giant cell. At the periphery of each lesion was a group of engorged capillaries (fig. 2).

The pia contained a few small tubercles, and was infiltrated with fibrin and densely packed masses of epithelioid and lymphoid cells and large mononuclear cells, with small, dense, eccentric nuclei.

The mass of cortical softening already described contained a small vessel in which was an organized thrombus undergoing canalization and about which were radiating epithelioid cells. The Virchow-Robin spaces were quite wide.

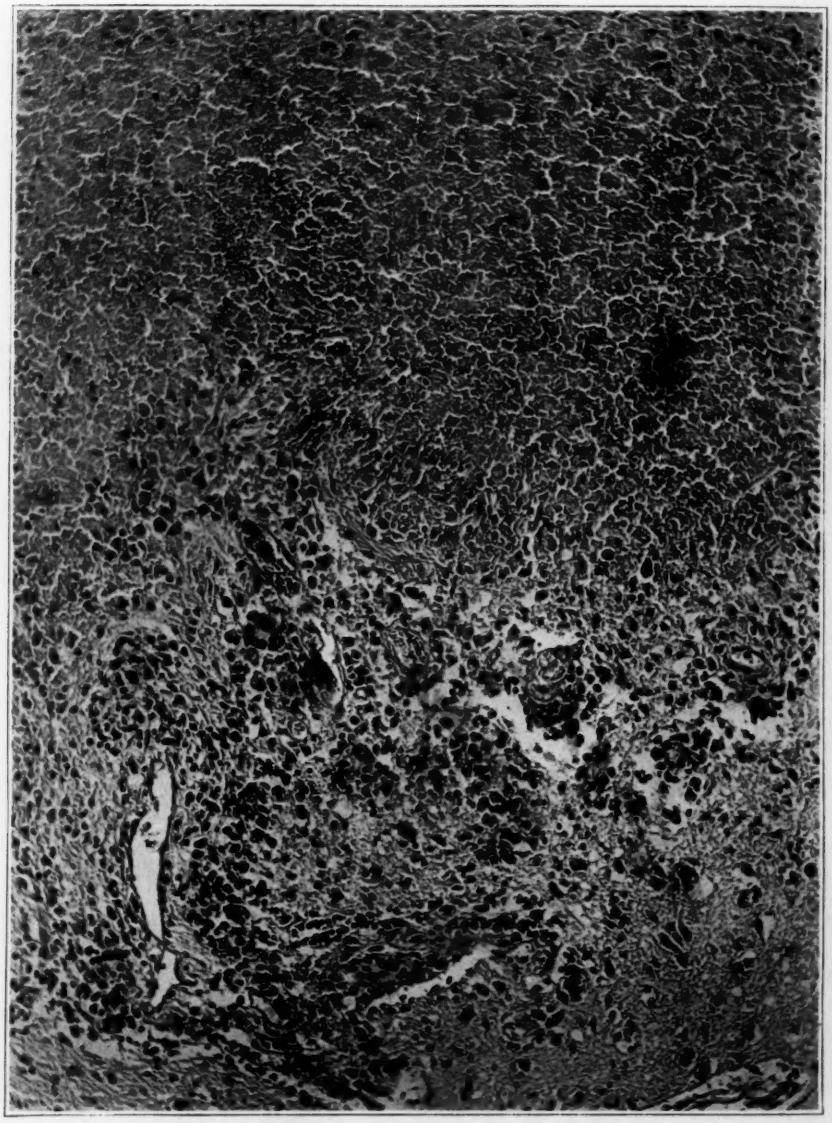

Fig. 3.—Cellular structure of the cerebral lesions.

A smear of the exudate from the base of the brain showed only acid-fast organisms. A culture of the blood made at necropsy showed no growth in seven days.

COMMENT

The pathologic picture was that of numerous pinhead to pea-sized solitary and conglomerate tubercles scattered throughout the entire brain, with some tuberculous meningitis, meningo-encephalitis, generalized miliary tuberculosis and tuberculosis of the tracheobronchial lymph nodes. The primary focus of the disease could not be determined.

While the clinical diagnosis was tuberculous leptomeningitis and miliary tuberculosis of the lungs, there was some deviation from the usual clinical course of tuberculous meningitis. The occurrence of a convulsion followed by trismus and loss of reflexes and the resemblance to tetanus were confusing in establishing a diagnosis.

The duration of the disease also was not typical. Six months elapsed from the onset of symptoms until death occurred, while a child with tuberculosis of the meninges usually dies in considerably less than half that time.

In the average patient with meningeal tuberculosis, the cells of the cerebrospinal fluid do not exceed 300 per cubic millimeter. In our patient, however, they increased from 120 to 1,730 per cubic millimeter before death occurred, and numbered more than 400 per cubic millimeter for three weeks. As usual, nearly all of the cells were lymphocytes. Only by the necropsy observations was the exact diagnosis established.

In our experience, small tuberculomas are not infrequently found in the brains of children dying of tuberculous meningitis. Such lesions are usually in the pons and are practically always single. According to Kaufmann,[8] "Occasionally larger tubercles of the cerebrum arise . . .; more rarely there are larger numbers in all parts of the brain. More frequently these solitary, or better, conglomerate tubercles, are independent of disease of the meninges, but develop slowly after tubercle bacilli have been distributed via the blood stream into the cerebral substance. . . . They reach the size of peas, hen's eggs, or apples." MacCallum[9] expressed the belief that in nearly every case of tuberculosis of the meninges some antecedent involvement of the brain can be found.

In our patient the first symptom suggestive of involvement of the central nervous system was a change in disposition. This was accompanied by fever, loss of weight and loss of appetite, which would at least suggest the possibility of a tuberculous process somewhere in the body.

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8. Kaufmann, Edward: Lehrbuch der pathologischen Anatomie, translated by Stanley P. Reiman, Philadelphia, P. Blakiston's Sons & Company, 1929.

9. MacCallum, W. G.: A Text-Book of Pathology, Philadelphia, W. B. Saunders Company, 1924.

Signs of meningeal involvement did not develop until five months later, but during the succeeding month, the course more closely resembled the usual clinical course of tuberculous meningitis.

Judging from the size attained by the lesions, those in the brain would seem to have existed longer than those in the meninges or other parts of the body, except those in the tracheobronchial lymph nodes. The latter may have been the source of tubercle bacilli that were distributed to the brain via the blood stream.

From the late development of the meningeal symptoms and the discrepancy in the age of the cerebral and meningeal lesions, we would infer that the early change in disposition which the child showed was the result of the parenchymatous involvement of the brain, and that, as Kaufmann [8] has stated, this involvement occurred independent of a later disease of the meninges.

The convulsive seizures and motor phenomena may have resulted from either a cortical lesion or from increased intracranial pressure incident to meningeal involvement. No explanation is offered for the large number of cells in the cerebrospinal fluid, but a similar condition has been observed in a patient with a solitary tuberculoma of the brain.

CONCLUSIONS

The clinical and pathologic picture presented in the case reported warrants a diagnosis of diffuse tuberculous encephalitis.

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CONGENITAL BONE DYSPLASIA (OSTEOGENESIS IMPERFECTA) ASSOCIATED WITH LESIONS OF THE PARATHYROID GLANDS*

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Lack of proper development of the osseous system in the new-born, commonly called osteogenesis imperfecta, occurs with sufficient frequency to have long stimulated wide interest. Recent studies relating the parathyroid glands to disease of the bone would seem to justify the presentation of the following case.

REPORT OF CASE

History.—The patient was a white girl, aged 4¼ weeks. The mother was 30 years old; the father, 31 years. It was the first pregnancy. There was no familial history of diseases of the bone, syphilis or tuberculosis. The diet of the mother was adequate throughout pregnancy. The baby was full term and was delivered normally. Her birth weight was 7¼ pounds (3,288 Gm.). There was moderate cyanosis for a short time after birth. The infant had been on dilutions of whole milk since birth. At birth it was noticed that the upper and lower extremities were deformed; the legs were flexed at the knees and hips and their extension was difficult. Because of these deformities the baby was taken to an orthopedic hospital and from there she was referred to the New York Nursery and Child's Hospital.

Physical Examination.—On admission her condition was poor, her weight being 1 ounce (28.3 Gm.) less than at birth. The color of the skin was cyanotic at times and ashen gray at other times. The deformities of the extremities are shown in figure 1. The skull was of parchment-like consistency, particularly over the occiput. The baby's condition gradually became worse, the cyanosis more marked and the respirations more rapid and difficult. A few hours before death, numerous small petechial hemorrhages appeared over the body, particularly over the anterior aspect of the chest and abdomen. The temperature was normal on admission, rising to 101.6 F. fifteen hours later, and to 103.6 F. prior to death, about forty hours following admission.

Laboratory Data.—Examination of the blood showed: erythrocytes, 3,250,000; hemoglobin, 86 per cent of normal for the infant's age; leukocytes, 20,400; polymorphonuclears, 52 per cent; large lymphocytes, 12 per cent; small lymphocytes, 36 per cent; serum calcium (Clark and Collip modification of the Tisdall method),

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* From the Department of Pediatrics, Cornell University Medical College, and the New York Nursery and Child's Hospital.

10.2 mg., and serum phosphorus (Tisdall method), 6.5 mg. per hundred cubic centimeters and serum protein, 5.72 per cent (Reiss); the Wassermann reaction of the blood and the tuberculin reaction were negative.

Roentgen Examination.—There was marked osteoporosis throughout the entire skeleton excepting the vertebral column. The shafts of the long bones showed

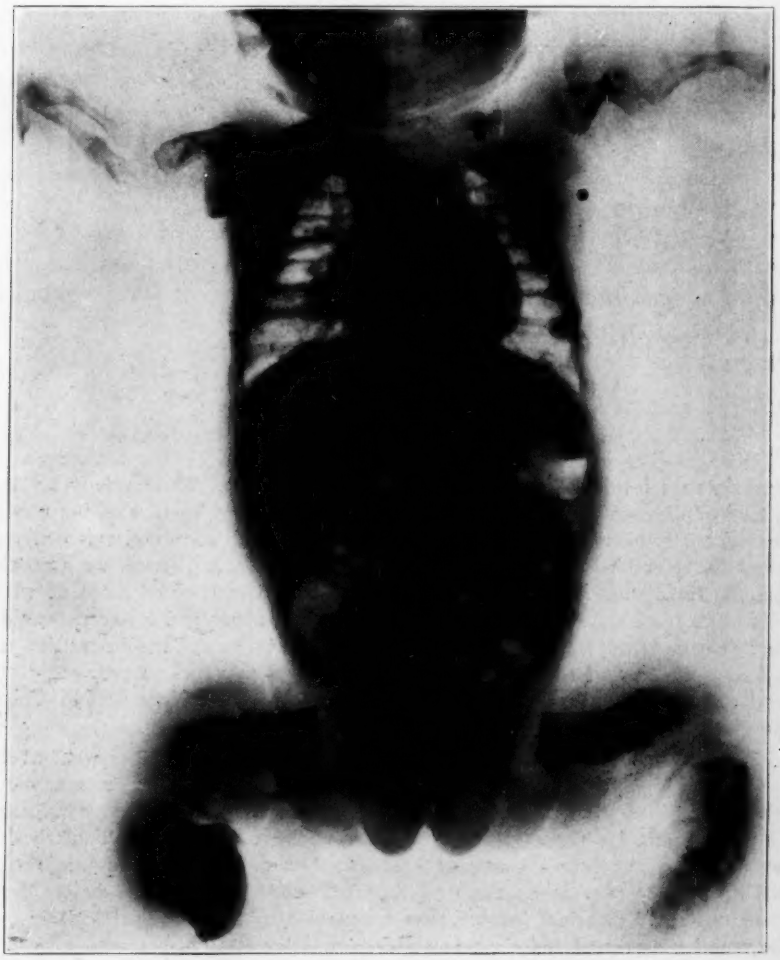

Fig. 1.—Roentgenogram of the skeleton. The osteoporosis and fractures are more clearly seen in the femora and humeri than elsewhere.

increase in width without increase in the thickness of the cortex. There were multiple fractures of the clavicles, ribs and long bones of both upper and lower extremities, with occasional callus formation of considerable density and amount. The bones of the skull, especially the parietal and occipital bones, showed patchy and imperfect calcification (fig. 1).

Autopsy.—External examination showed deformities of the extremities, softness of the skull and numerous scattered petechial hemorrhages in the skin. The

Fig. 2.—A posterior view of the organs of the neck. The two superior parathyroid glands are seen as black nodules (*A* and *B*) on the posterior aspect of the lateral lobes of the thyroid gland.

Fig. 3.—Photomicrograph showing the structure of the two superior and right inferior parathyroid glands. The large peripheral zone is a blood space which is continuous at *A* and *B* with the large capillaries in the glandular tissue. A septum across the peripheral sinus is shown at *C*.

peritoneal, pleural and pericardial cavities, mediastinum and heart were essentially normal. The lungs were normal except for slight evidence of widespread atelectasis. The spleen, liver, kidneys, suprarenal glands and organs of the pelvis were essentially normal. The organs of the neck were normal except for the parathyroid glands; the two superior and right inferior parathyroid glands were from 2.5 to 3 mm. in diameter and stood out sharply as well defined, dark bluish-red, beadlike masses in distinct contrast to the underlying grayish-red lobes of the thyroid gland. The left inferior gland was 1.5 mm. in diameter and was of the

Fig. 4.—Higher magnification of a band of glandular tissue with a large blood space on each side. Well preserved erythrocytes are seen adjacent to the glandular tissue. The black granular material represents "formalin pigmentation" in the blood. A portion of a large capillary may be seen at *A;* one of more normal size at *B*.

normal pale reddish-brown color except for one or two pinpoint reddish dots on its surface (fig. 2).

The brain showed areas of old hemorrhage, 1.5 and 2 cm. in diameter, in the right parietal and left occipital lobes, respectively. These areas were well defined and marked off from the surrounding brain tissue. The osseous system showed a marked lack of calcification with numerous fractures of the ribs and long bones.

Large soft calluses were present at some of the fractures. In the long bones there were relatively large areas which showed almost no gross calcification. (Such an area in the right humerus had been interpreted in the roentgenogram as suggesting the possibility of cyst formation.) The skull showed thinning and irregular patchy calcification, most marked in the parietal and occipital bones.

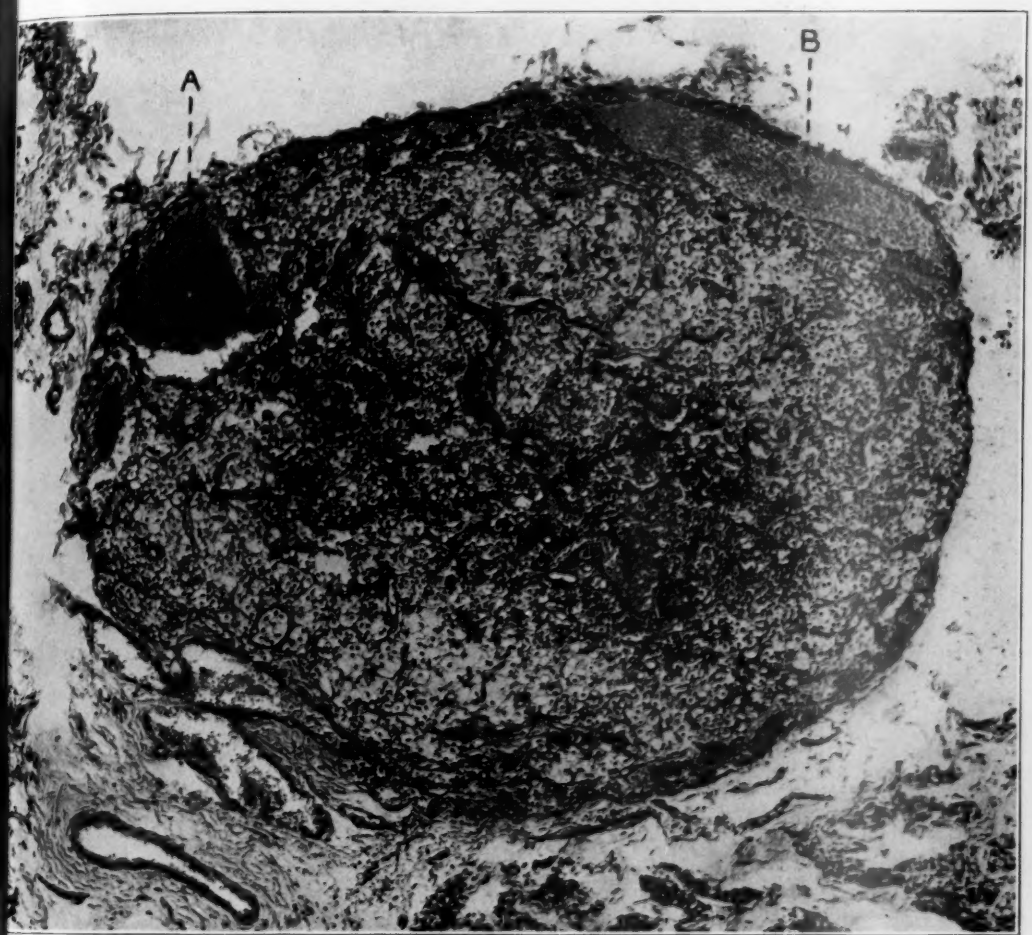

Fig. 5.—The left inferior parathyroid gland which is essentially normal except for the two large blood spaces shown at *A* and *B*.

Microscopic Examination.—Parathyroid Glands: The two superior and right inferior glands consisted largely of enormous sinus-like blood spaces which surrounded and extended into the relatively small masses of glandular tissue. These peripheral spaces were separated from the connective tissue capsules of the glands by a compressed layer of epithelial cells, usually one or two cells in thickness. At irregular intervals this layer of cells, carrying with it a small amount of connective tissue from the capsule, bridged across the blood spaces and was continuous

with the central mass of parenchymal tissue. These septal trabeculae appeared to be comparable to those which occur in relation to the peripheral lymph sinuses of normal lymph nodes. In addition to the large blood spaces which extended into the substance of the glands from the peripheral sinuses, there were the small thin-walled capillaries which are normally present. That the large peripheral sinuses represented channels for circulating blood, and not hemorrhage, was evident in that they were definitely continuous in certain planes of section with the large capillaries of the gland tissue itself. They showed no evidence of throm-

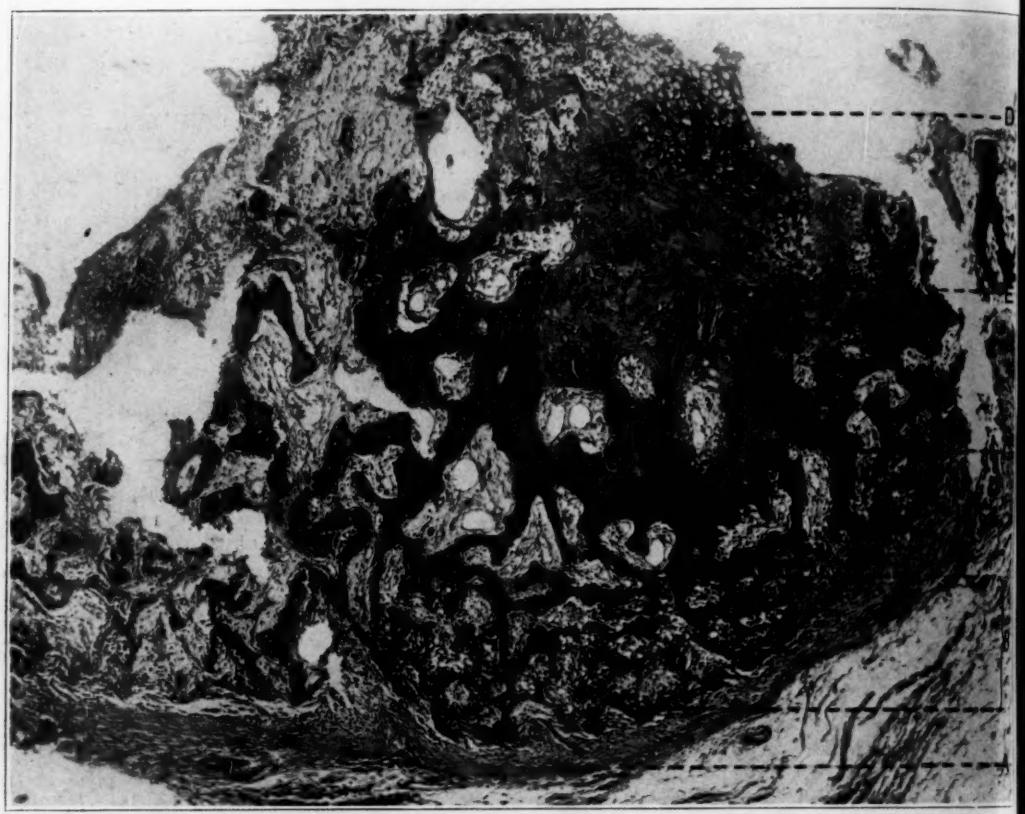

Fig. 6.—Section from the diaphysis of the right humerus. *A*, periosteum; *B*, zone of active osteoblastic differentiation; *C*, osteoid tissue; *D* immature cartilage; *E*, partially necrotic osteoid tissue and cartilage.

bosis, and well preserved erythrocytes could be seen at the peripheries of the sinuses where the clot (post mortem) was thinnest. The structure of these three glands is shown in figures 3 and 4. The fourth gland, the left inferior (fig. 5), was normal in structure except for two large capillaries at the periphery. The parenchymal cells themselves in all four glands showed no recognized variation from the normal structure (fig. 5).

Osseous System: Sections from various portions of the long bones showed fairly marked osteoblastic activity with the formation of rather large amounts of

vascular "fibroblastic osteoid tissue." The staining of the osteoid tissue showed it to contain very small amounts of calcium salts, and only occasionally did it resemble true bone (figs. 6 and 7). The osteoblastic acivity was most marked in the region of the periosteum, the connective tissue deeper in the bone showing considerably less differentiation. A tendency toward necrosis of the poorly calcified osteoid tissue was a prominent feature of all the sections. In some areas the inflammatory reaction to this necrosis, particularly in the presence of appreciable calcification, was such that it resembled the changes of osteitis fibrosa with a

Fig. 7.—Higher magnification of a portion of zone *B*, figure 6, showing active osteoblastic activity with the formation of osteoid tissue. The upper right portion of the section shows beginning necrosis of the osteoid tissue.

foreign body giant cell reaction (figs. 8 and 9). The attempts at repair of the fractures was essentially that which normally occurs in so far as osteoblastic differentiation was concerned; however, calcification of the osteoid tissue was slight. Islands of immature cartilage were scattered through the osteoid tissue. Sections of the skull consisted of a thin layer of cellular osteoid tissue occurring in irregularly scattered segments which were separated by connective tissue. The osteoblastic activity was, in general, less marked in the skull than has been described in the long bones, except in certain areas between the patches of osteoid

tissue. This lack of osteoblastic differentiation together with the thinness of the bones of the skull resembled more the picture of faulty mesoblastic development than did that seen in the diaphyses of the long bones.

Chemical analysis of the bone ash showed: calcium, 34.2 per cent (Kramer and Shear method); phosphorus, 16.7 per cent (magnesium ammonium phosphate method), and sodium, 1.211 per cent (Fiske method, unpublished). Examination of the bone ash of a normal infant of about the same age, using the same methods, showed: calcium, 35.3 per cent; phosphorus, 17.9 per cent, and sodium, 0.836 per cent.

Fig. 8.—Section from the diaphysis of the right humerus showing fibrosis and inflammatory reaction to necrosis. Numerous giant cells (osteoclasts) are present (*A*).

SUMMARY OF THE LITERATURE

Parathyroid Glands and Bone Disturbances.—It has long been known that accidental or experimental removal of the parathyroid glands causes a lowering of the blood calcium, an increase of the blood phosphorus and tetany. The isolation of parathormone by Collip made it possible to produce experimentally the changes which are now recognized as indicating hyperparathyroidism. This clinical entity, usually

accompanying an adenomatous tumor of one or more glands, has been carefully studied and reported by many observers.[1] These studies seem to indicate beyond question that the syndrome of hyperparathyroidism is characterized by:

1. A definite increase in the excretion of calcium and phosphorus, almost entirely in the urine.

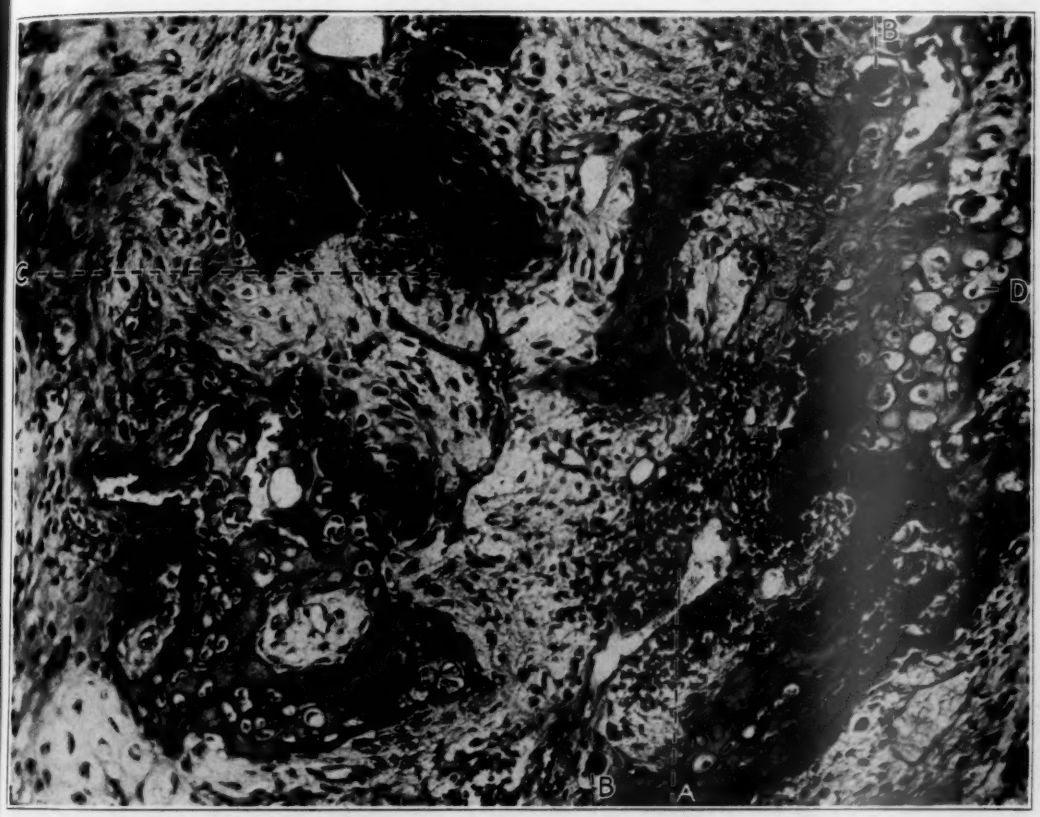

Fig. 9.—Higher magnification of the field outlined in figure 8. *A*, inflammatory reaction to necrosis of osteoid tissue; *B*, giant cells (osteoclasts); *C*, osteoblasts, and *D*, cartilage cells.

1. Hannon, R. R.; Shorr, E.; McClellan, W. S., and DuBois, E. F.: Case of Osteitis Fibrosa Cystica (Osteomalacia?) with Evidence of Hyperactivity of Parathyroid Bodies: Metabolic Study, J. Clin. Investigation **8**:215 (Feb.) 1930. Bauer, W.; Albright, F., and Aub, J. C.: Case of Osteitis Fibrosa Cystica (Osteomalacia?) with Evidence of Hyperactivity of Parathyroid Bodies: Metabolic Study, ibid. **8**:229 (Feb.) 1930. McClellan, W. S., and Hannon, R. R.: Case of Osteitis Fibrosa Cystica (Osteomalacia?) with Evidence of Hyperactivity of Parathyroid Bodies: Metabolic Study, ibid. **8**:249 (Feb.) 1930. Barr, D. P., and Bulger, H.

2. A definite increase in serum calcium.
3. A decrease in serum phosphorus.
4. A negative calcium balance.
5. A depletion of the calcium content of bone.

The importance of the last of these factors is emphasized by the fact that of the seventy-four cases of pathologically enlarged parathyroid glands which Barr and Bulger [2] collected, forty-five showed some form of disease of the bone; thirty-two of these forty-five patients had generalized osteitis fibrosa cystica. There is sufficient fundamental similarity between the histopathology of osteitis fibrosa and that seen in certain sections of the bones in this case to suggest that the two conditions may have certain elements in common.

On the other hand, there is evidence to suggest that during periods of growth or repair, a partial or complete lack of parathyroid function inhibits the deposition of calcium in the osteoid tissue, with a simultaneous decrease in the calcium content of the blood.[3]

Osteogenesis Imperfecta.—The term osteogenesis imperfecta, as it is commonly used, refers to any congenital disturbance that results in bone of poor quality. The degree of the disturbance and its compatability with life vary between wide limits. A comprehensive review of the voluminous literature is unnecessary in this paper since such a summary was recently given in a paper by Dietrich.[4] Nothing is definitely known concerning its etiology. In a recent paper Weber [5]

A.: Clinical Syndrome of Hyperparathyroidism, Am. J. M. Sc. **179**:449 (April) 1930. Albright, F.; Bauer, W.; Ropes, M., and Aub, J. C.: Calcium and Phosphorus Metabolism; Effect of Parathyroid Hormone, J. Clin. Investigation **7**:139 (April) 1929. Albright, F., and Ellsworth, R.: Calcium and Phosphorus Studies on Case of Idiopathic Hypoparathyroidism, ibid. **7**:183 (June) 1929. Richardson, E. P.; Aub, J. C., and Bauer, W.: Parathyroidectomy in Osteomalacia, Ann. Surg. **90**:730 (Oct.) 1929. Boyd, J. D.; Milgram, J. E., and Stearns, G.: Clinical Hyperparathyroisim, J. A. M. A. **93**:684 (Aug. 31) 1929. Wilder, R. M.: Hyperparathyroidism: Tumor of Parathyroid Glands Associated with Osteitis Fibrosa, Endocrinology **13**:285 (May-June) 1929. Hoag, L. A.; Rivkin, H.; Weigele, C. E., and Berliner, F.: Effect of Potent Parathyroid Extract on Calcium Balance in Infants, Am. J. Dis. Child. **33**:910 (June) 1927. Hunter, D.: Hyperparathyroidism, Proc. Roy. Soc. Med. (Sect. Med.) **23**:27 (Dec.) 1929. Compere, E. L.: Bone Changes in Hyperparathyroidism, Surg., Gynec. & Obst. **50**:783 (May) 1930.

2. Barr and Bulger (footnote 1).

3. Dragstedt, L. R.: The Physiology of the Parathyroid Glands, Physiol. Rev. **7**:499, 1927.

4. Dietrich, A.: Die Entwicklungsstörungen des Knochens, in Henke and Lubarsch: Handbuch der speziellen Pathologie und pathologischen Anatomie, Berlin, Julius Springer, 1929, vol. 9, p. 198.

5. Weber, M.: Osteogenesis Imperfecta Congenita: Study of Its Histopathogenesis, Arch. Path. **9**:984 (May) 1930.

concluded that the disease represents a congenital malformation of the bone-building system. On the other hand, Fahr [6] explained the disease on the basis of a generalized disturbance of the endocrine system, this being suggested by what seemed to be disproportionate development of the endocrine glands. He also found in his case small petechial hemorrhages in the parathyroid glands which he was inclined to disregard because of the frequency with which they are found in other conditions. Because of Fahr's [6] observations, Kraus [7] made a careful study of all the endocrine glands in his case and, in the absence of pathologic observations, concluded that the disease was the result of a disturbance in the mesoblastic tissue. Knaggs [8] and Fairbank [9] in their reviews were inclined toward the same view concerning the etiology as Weber and Kraus. Fairbank, however, found it difficult to explain the healing of fractures if primary lack of osteoblastic differentiation caused the disease. He suggested that further work with phosphatase such as Robison and his associates have been doing may throw considerable light on the whole problem.[10]

The calcium and phosphorus studies of osteogenesis imperfecta which have been reported are inconclusive. Bookman,[11] in a metabolic study of one patient, aged 10 weeks, found that although there was a slight decrease in the calcium retention as compared with the normal, a positive calcium balance was still maintained. He suggested that the calcium balance may vary a great deal at different times depending on the variable activity of the different factors involved. Sindler,[12] in a study of a 20 day old infant, found the metabolism of nitrogen, fat, calcium, phosphorus, magnesium, potassium and chlorides to be normal. His analysis of the bone ash showed a decrease in the amount of calcium, an increase in the phosphorus and an enormous increase in the sodium. Schwarz and Bass [13] reported a normal nitrogen, calcium

6. Fahr, T.: Ueber Osteogenesis imperfecta, Virchows Arch. f. path. Anat. **261**:732, 1926.

7. Kraus, E. J.: Osteogenesis imperfecta und endokrines System, Virchows Arch. f. path. Anat. **274**:37, 1929.

8. Knaggs, R. L.: Osteogenesis Imperfecta (Hunterian Lecture, R. C. S.), Brit. J. Surg. **11**:737 (April) 1924.

9. Fairbank, H. A. T.: Some Remarks on Osteogenesis Imperfecta (President's Address), Proc. Roy. Soc. Med. (Sect. Dis. Child.) **23**:77 (July) 1930.

10. Fell, H. B., and Robison, R.: The Growth, Development and Phosphatase Activity of Embryonic Avian Femora and Limb Buds Cultivated in Vitro, Biochem. J. **23**:767, 1929.

11. Bookman, A.: The Metabolism in Osteogenesis Imperfecta with Special Reference to Calcium, Am. J. Dis. Child. **7**:436 (Dec.) 1914.

12. Sindler, A.: Der Stoffwechsel bei Osteogenesis imperfecta, Ztschr. f. Kinderh. **42**:85, 1926.

13. Schwarz, H., and Bass, M.: Osteogenesis imperfecta: Report of a Case with the Study of Its Metabolism, Am. J. Dis. Child. **5**:131, 1913.

and phosphorus metabolism. Flagstad, Zanger and Leven [14] and Tisdall, Howland and Kramer [15] also reported essentially normal values for the calcium and phosphorus content of the blood in osteogenesis imperfecta.

COMMENT

It is unfortunate that a complete study of the calcium balance could not be made because of the early death of the patient after her admission to the ward. The normal calcium and phosphorus values in the blood were in accord with those reported in osteogenesis imperfecta. They do not suggest a parathyroid disturbance. However, these bones presumably never had their normal content of calcium salts and this could possibly explain calcium and phosphorus levels in the blood which differ from those characterizing the parathyroid disturbances of later life.

The content of calcium and phosphorus in the bone ash and the ratio between them was normal. The definite increase in the amount of sodium in the ash suggests, as one would expect, a relative decrease in the amount of calcium phosphate per unit of bone.

The histopathologic changes of the bones in some sections, particularly those of the skull, resemble somewhat the description of osteogenesis imperfecta by Weber, from which he concluded that the disease represents a primary lack of normal mesoblastic development. However, the osteoid tissue in this case tended to be more abundant and showed less evidence of calcification, suggesting that the case may have differed in some fundamental way from those which he described.

A search of the literature has revealed no description of such a lesion of the parathyroid glands as that found in this case. In a histologic study of 815 parathyroid glands from 240 autopsies on subjects of all ages, from a 7 months fetus to a person 80 years old, Kurokawa [16] found no such lesion.

One is given the definite impression from the sections of the parathyroid glands in this case that there was a smaller amount of gland parenchyma than normal; however, the question can be raised as to the possible influence of such great vascularity on the amount of secretion absorbed into the blood. In view of the conflicting experimental evidence, it would seem that the changes in the bones in this case could have resulted from either decreased or increased parathyroid

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14. Flagstad, A. E.; Zanger, E., and Leven, L.: Osteogenesis Imperfecta: Blood Chemistry Study; Preliminary Report, Minnesota Med. **7**:800, 1924.

15. Tisdall, F. F.; Howland, J., and Kramer, B.: The Clinical Significance of Calcium Concentration in the Serum of Children and Possible Errors in Its Determination, Am. J. Dis. Child. **22**:560 (Dec.) 1921.

16. Kurokawa, K.: Histological Studies of Normal and Pathological Parathyroid Glands (Human), Japan M. World **5**:241 (Sept.) 1925.

function during the period of growth. On the other hand, the bone dysplasia and the changes in the parathyroid glands may be purely coincidental. The possibility exists, however, that certain cases of so-called "osteogenesis imperfecta" may be the result of congenital parathyroid disturbances and not primarily the result of mesoblastic malformation, although the two may be associated in some unknown way. The comparatively recent interest in pathologic changes in the parathyroid glands related to disease of the bone will undoubtedly result in more careful examination of the parathyroid glands in all types of bone disturbance.

SUMMARY

A case is described in which there was marked congenital bone dysplasia and unusual vascularity of the parathyroid glands with a relatively small amount of parenchymal tissue. A brief review of osteogenesis imperfecta and the relation of the parathyroid glands to disease of bone is given. The possibility is suggested that so-called "osteogenesis imperfecta" may sometimes be based in part on a congenital parathyroid disturbance rather than be purely the result of faulty mesoblastic differentiation.

Progress in Pediatrics

NUTRITION OF THE DENTAL TISSUES*

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Nutrition of the dental tissues is still a virgin field, for few investigators admit its presence or necessity. All investigators realize the importance of a properly balanced diet during the period of formation of teeth, but the question of whether this continues to apply after the completion and eruption of the teeth is, as yet, under active discussion. Histologists generally do not believe this to be the case, for no system of channels joining the enamel with the vascular system of the body is believed to exist. To prove that such a system exists is my purpose in this paper.

There has been much discussion in the literature concerning the effect of diet on the welfare of the teeth. An investigator who has contributed greatly to this subject is Dr. Percy R. Howe[1]; he was able to develop dental decay in monkeys fed on deficient diets. Much more work must be done, however, before it will be possible to state the specific elements necessary to dental health and those harmful to the teeth. Not only are these unknown, but the manner in which an unbalanced diet can effect the welfare of fully formed teeth is not understood.

There are two means by which food may affect the teeth: (1) from the exterior by means of the saliva, and (2) from the interior by means of the blood.

(1) Twenty years ago the saliva was considered to be the most important factor influencing the activity of dental decay. Many chemical analyses were made of this fluid in the hope of finding a chemical difference between that secreted in the mouths of immune persons and that of persons susceptible to dental decay. Some differences were found, but it was further discovered that the saliva is exceedingly changeable in the same persons during even a single day. The figures obtained from these analyses, however, rarely showed definite uniformity; there-

* Read before the meeting of the Section of Pediatrics of the New York Academy of Medicine, Feb. 11, 1931.

1. Howe, Percy R.: Studies of Dental Disorders Following Experimental Feeding in Monkeys, J. Am. Dent. A. **11**:1149 (Dec.) 1924.

fore no specific constituents of the saliva could be regarded as necessary in maintaining dental health. The varying hydrogen ion concentration of the saliva is not now regarded as a direct menace to the teeth, for the p_H of the free saliva rarely drops so low as to decalcify the enamel. If it did, decay would attack all surfaces of the teeth—a clinical picture not noted in true dental decay.

Nutritional unbalance may possibly cause some change in the saliva (such as the formation of antibodies), which may hinder the development of aciduric organisms in the mouth. This type of organism is held responsible for the decay of teeth by Bunting,[2] Rodriguez,[3] McIntosh and his associates [4] and others. If it is shown that the saliva may be thus affected, the exciting cause of dental decay, that is, the formation of acids in the mouth, can disappear, and the disease be brought to a standstill. I believe, however, that dental decay has not only an exciting cause affecting the teeth from the exterior, but a predisposing cause originating in the interior.

(2) Teeth may be affected from the interior by the blood or the lymph.[5] This appears to be a plausible predisposing cause of dental decay, since these elements influence the nutrition of the teeth. Yet it has been maintained that fully erupted teeth do not require nutrition. This erroneous conception is due to the lack of fundamental data concerning the histologic structure of the dental tissues.

Teeth are considered to be uninfluenced by systemic disorders and regarded as organs entirely separate from the body. Consequently, dental decay has been treated mainly from the reparative angle instead of from the standpoint of true prevention. This nonvitalistic view of the teeth is biologically unfounded, for all tissues that are permanently retained in the body require some form of nourishment, and in the end the dental organs will prove to be no exception to this biologic rule; they will be shown to be in vital relationship to the body.

All teeth are furnished with nourishment by blood vessels in the dental pulp, which are particularly profuse during youth. Such a supply of blood must have a function, for nature does not maintain an organ in a state of uselessness. Examinations of the pulps of teeth

2. Bunting, R. W.: Rôle of Bacillus Acidophilus in Dental Caries, J. Am. Dent. A. **12**:381, 1925.

3. Rodriguez, F. E.: A Method of Determining Quantitatively the Incidence of Lactobacillus Acidophilus Odontolyticus in the Oral Cavity, J. Am. Dent. A. **15**:1711, 1928.

4. McIntosh, J.; James, W. W., and Lazarus-Barlow, P.: An Investigation into the Etiology of Dental Caries: The Biological Characteristics and Distribution of B. Acidophilus Odontolyticus; Further Experiments on the Production of Artificial Caries, Brit. J. Exper. Path. **5**:175, 1924.

5. Bödecker, C. F.: Nutrition of the Enamel of the Human Teeth, Dental Cosmos **53**:1000 (Sept.) 1911.

show that these organs are particularly well supplied with blood during youth. It may be more than a mere coincidence that dental decay is most active in the teeth of young persons living on the highly refined food of the present day. Dr. Howe [1] has shown that some malnutritional conditions of the body can be reflected in the dental pulp (as in other tissues); thus its function is disturbed, which causes the teeth to become more susceptible to decay.

As the presence of blood in other tissues of the body indicates that metabolism is active, it is quite plausible to assume that the blood in the dental pulp fulfils a like function. I believe that the purpose of the dental pulp is to furnish nutritive material for the teeth. While this may seem to many to be self-evident, it is by no means an accepted truth.

A brief description of the newer conception of the histologic structure of the teeth is necessary in order to show the channels by which the dental tissues supposedly receive their nourishment. I realize fully that the teeth necessitate a different type of nourishment from that required by the more highly differentiated tissues of the body. The principal elements that the teeth probably require to fulfil their function satisfactorily are mineral salts and possibly fat. These elements would make the teeth more resistant to the decalcifying action of the oral acids and maintain the dental tissues immune to decay.

CHANNELS OF THE DENTAL LYMPH

The nutritive fluid of the teeth originates in the blood of the dental pulp and is secreted by the odontoblasts of this organ (fig. 1, *A* and *B*). The provisional term that has been selected for this fluid secreted by the odontoblasts is dental lymph.[6] I realize that such a designation may give a wrong impression of the character of this fluid, for its chemical constitution is probably different from that of body lymph, just as other glandular secretions are different from the blood from which they are selected.

Abnormal variations in the chemical constituents of the dental lymph may be effected by at least two means: (1) the reduction of the essential elements in the blood plasma, owing to malnutritional conditions of the body, and (2) the malfunctioning of the secretory odontoblasts, rendering them unable to select the proper elements even if present in the blood plasma. Either or both of these conditions result in a subnormal dental lymph.

The odontoblasts are columnar cells, from 25 to 30 microns long and 5 microns wide, covering the surface of the pulp in a single layer (fig. 1*B*). They each have one long process which passes into

6. Bödecker, C. F.: A New Theory of the Cause of Dental Caries, Dental Cosmos **71**:586 (June) 1929.

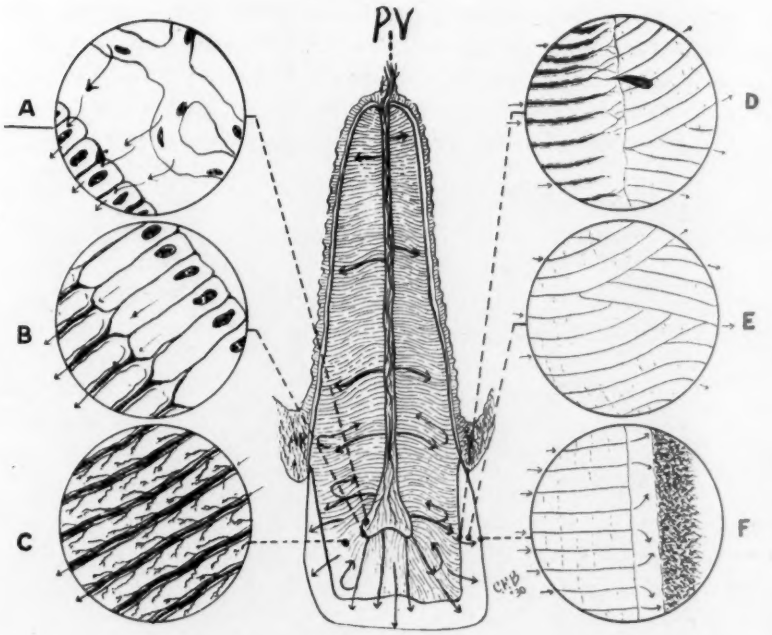

Fig. 1.—Nutritional channels of the dental tissues. The central figure is a diagram of an axial section of a maxillary incisor showing the entrance of blood vessels and nerves (*PV*) at its apex. The dentin (shown in delicate radial lines, the dentinal tubules) forms the bulk of the tooth, the crown being covered by a variable thickness of enamel. Heavily marked arrows, radiating from the central canal and containing the dental pulp ("nerve"), show the general direction of the flow of the dentinal lymph. Under normal conditions of health, this is believed to be circulatory in the dentin and outward only in the enamel (shown by delicate arrows on the margin of *A* to *F*). *A* is a high magnification of a part of the dental pulp near its surface. Blood plasma is diffusing through the walls of a capillary thus surrounding the odontoblasts, the secretory cells of the dental pulp. *B* is the margin of the pulp and surrounding dentin. The columnar odontoblasts select essential elements from the blood plasma and convey this fluid, the dentinal lymph, into the dentin by way of their "fibrils." *C* is the dentin with its innumerable channels containing the "fibrils" of the odontoblasts and their delicate lateral branches which serve to distribute the dentinal lymph; these fibrils are tubular. *D* is the dentino-enamel junction. The dentinal "fibrils" end in forked branches and pass the lymph to the enamel rod sheaths which envelop each enamel rod. *E* shows the central portions of the enamel and the passage of the dental lymph through the enamel rod sheaths. *F* shows the surface of the enamel with its cuticle, and at the right, the adhering mucous plaque, food débris and bacteria. Acid is supposed to be generated by the bacterial fermentation of carbohydrate food which decalcifies the enamel. During youth when the teeth are highly permeable, in healthy conditions the mineral content of the dentinal lymph acts as a buffer, thus preventing the decalcification of the enamel by acids in the mouth. An insufficiency of mineral salts or of dentinal lymph during youth results in dental decay. This complex system of channels supplies both the dentin and the enamel of young teeth with mineral salts and possibly with fat essential for dental health.

the dentin, called the dentinal fibril or the fiber of Tomes. These dentinal fibrils run in minute channels, the dentinal tubules, of which there is a countless number (fig. 1*C*), having a diameter of 2 microns. At frequent intervals, the dentinal fibrils give off delicate lateral branches that pass into the basic substances of the dentin.

Fig. 2.—Unstained ground-section of a tooth at the dentino-enamel junction photographed with ultraviolet light. The profusion of the terminal endings of the dentinal tubules is well suited to distribute lymph to the enamel. *E* represents the enamel and *D* the dentin.

A misconception has long been held concerning the structure of the dentinal fibrils; they are not fibers, as has been generally believed, but are in the form of tubes containing a fluid.[7] Instead of fibrils such a

7. Bödecker, C. F.: The Soft Fiber of Tomes, a Tubular Structure, J. Nat. Dent. A. **9**:281 (April) 1922.

system of tubes naturally permits the transportation of a greater amount of dental lymph. A careful microscopic examination of dentin treated with suitable stains shows it to contain an exceedingly intricate system of channels which distributes the lymph to the dentin.

A photomicrograph taken with ultraviolet light of a ground-section of a tooth at the dentino-enamel junction shows that the dentinal tubules

Fig. 3.—Photomicrograph of a ground-section of a tooth, showing the distribution of the tufts (*T*) at the dentino-enamel border. These structures serve to distribute lymph to the enamel rod sheaths which are barely perceptible under this low magnification. *E* stands for enamel and *D* for dentin.

usually end in delicate forked branches (fig. 2). These probably serve to transmit the dental lymph to the organic or protein structures of the enamel (fig. 1*D* and fig. 4).

Thus the enamel of the teeth also receives its quota of dental lymph for its calcification and protection, the quantity probably depending on

the age of the individual. Immediately after the eruption of the teeth, both the dentin and the enamel are in a state of high permeability; the age at which this is reduced, and possibly completely stopped, is not yet definitely known.

The principal structures in the enamel which take up the dental lymph from the terminal branches of the dentinal tubules at the border of these two tissues are the tufts, the enamel rod sheaths and the enamel lamellae.

The distribution of the enamel tufts is somewhat irregular, the majority being found on the eminences of the cusps of the dentino-

Fig. 4.—Photomicrograph of decalcified enamel. The mineral salts have been removed by the celloidin decalcifying method, leaving only the organic matrix which here consists of enamel rod sheaths. These appear to be the end-organs for the distribution of the dental lymph to the enamel.

enamel junction, penetrating the enamel for from one sixth to one fourth of its thickness. They arise from a narrow base and spread in a fanlike fashion, fraying out into the cement substance which holds the enamel rods together (fig. 3). That these structures are permeable to fluids during the life of an individual is indicated by laboratory experi-

ments,[8] by the experiments on animals performed by Fish[9] and by a photomicrograph of a specimen published by Howe.[10] This author showed a ground-section of a tooth from a person who died of lead poisoning; the lead is seen to have penetrated not only the dentin but the enamel tufts and lamellae.

The enamel rod sheath[11] is a delicate membrane enclosing each enamel rod (fig. 4). As the enamel is composed of a great number of minute columns having a diameter of about 4 microns, the enamel rod sheath excellently serves the purpose of distributing the dental lymph throughout this tissue by diffusion.

I have thus far described the dental lymph from the time of its secretion by the odontoblasts, through its conveyance into the enamel by the dentin, and finally, to the surface of the tooth. In the teeth of the young this area is covered by a thin, dense, resistant membrane, termed the enamel cuticle.

Figure 1*F* shows a diagram of the outer ends of the enamel rods covered by the enamel cuticle. A mucous plaque containing food débris, bacteria and mucus is seen attached to the surface of the cuticle. Such plaques are supposed to form an acid (some claim it to be lactic, others malic) because of the fermentation of particles of carbohydrate food. If the surface of the tooth is not protected by some means, the acid will attack the mineral salts of the enamel and thus initiate dental decay. Such a protection is probably achieved during youth in the following manner.

The presence of mineral salts in the dental lymph may neutralize the acid on the surface of the tooth and thus prevent its decay. This protective condition is particularly active in teeth during youth, when the dental tissues are in a state of high permeability. The possibility that the dental lymph might have a buffer power in neutralizing acids in the mouth was suggested to me as a result of a conversation with George W. Clapp, who believed that, as eating oranges developed a slight alkalosis, it might be possible to use this means to combat dental decay. The power of neutralizing an acid ascribed to the dental lymph is by no means unique in the physiologic reactions of the body. A close analogy is found in the neutralization of sarcolactic acid in the muscles achieved principally by the sodium bicarbonate in the blood plasma.

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8. Bödecker, C. F.: Permeability of the Enamel in Relation to Stains, J. Nat. Dent. A. **10**:60, 1923.

9. Fish, E. W.: The Circulation of Lymph in Dentin and Enamel, J. Nat. Dent. A. **14**:804, 1927.

10. Howe, Percy R.: A New Research on Dental Caries, Dental Cosmos **68**: 1021, 1926.

11. Bödecker, C. F.: Enamel of the Teeth, Decalcified by the Celloidin Decalcifying Method and Examined by Ultra-Violet Light, Dental Rev. **20**: (April) 1906.

There are two or possibly three functions of the dental lymph active in this manner in the teeth of the child and young adult: (1) to complete the calcification of the newly erupted teeth by furnishing mineral salts and fats; (2) to act as a buffer against external, destructive acids, and (3) possibly to discourage the growth of aciduric organisms in the mouth.

Newly erupted teeth are incompletely calcified; they require a further quota of mineral salts in order to attain their normal hardness. For this purpose calcific salts and possibly fat are conveyed to both the enamel and the dentin by the dental lymph. When calcification has been completed, probably between the ages of 20 and 30 years, the dental pulp reduces its activity, as indicated by cellular changes. Thus the quantity of the dental lymph is greatly reduced and sometimes brought to a complete standstill. The teeth of the adult are probably protected from decay after this time by their fat content, which is discussed elsewhere.

CONCLUSION

Dental decay will be recognized as a disease of an infectious origin, which is destroying the teeth of from 90 to 95 per cent of civilized peoples. The presence of the disease as well as the speed with which it attacks the dental tissue varies in different persons, according to some as yet only dimly recognized systemic conditions. The exciting cause of dental decay is probably an acid, generated by the bacterial fermentation of particles of carbohydrate food. For this reason the use of the toothbrush is essential, for the cleaner the teeth are kept, the less acid will be generated in the mouth. Besides the exciting cause of dental decay, however, a predisposing cause or causes exist. One of these will be found in the abnormal constitution of the dental lymph developed by the malfunctioning of the pulp and by deficiencies of the blood. A normal dental lymph protects the teeth of the young healthy person against decay. It is therefore believed that the teeth possess a protective mechanism against this disease, the activity of which is in all likelihood dependent on the health of the body. In this relation the diet of a person is doubtless an all important factor.

A number of practical observations of the effect of optimal diets on the reduction of dental decay have already been made by Bunting,[12] Boyd and Drain,[13] Mellanby,[14] McBeath and others. These have given

12. Bunting, R. W.: Certain Considerations in the Problem of Dental Caries, Am. J. Dis. Child. **40**:536 (Sept.) 1930.

13. Boyd, J. D., and Drain, C. L.: The Arrest of Dental Caries in Childhood, J. A. M. A. **90**:1867 (June 9) 1928.

14. Mellanby, May: Experiments on Dogs, Rabbits and Rats, and Investigations on Man Which Indicate the Power of Certain Food Factors to Prevent and Control Dental Diseases, J. Am. Dent. A. **17**:1456 (Aug.) 1930.

a general idea of what constitutes an optimal diet, but much is still to be learned. Possibly more progress might be made if biochemical analyses of the dental lymph could be performed, defining its exact constitution in teeth immune to decay and in those susceptible to it; then it might be possible to determine the elements essential to dental health. Work by a group financially assisted by the Commonwealth Fund of New York is progressing along this line in the Dental School of Columbia University.

Dental decay has been regarded in the past as resulting from local conditions in the mouth, which could be combated only by oral hygiene and by reparative means. As long as this belief is retained, little progress can be made in combating this ever-increasing scourge. It is my belief that dental decay is merely a symptom of some systemic disorder in the individual, and that when recognized, its occurrence gives an early warning of such a condition.

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THE RELATION OF BIRTH TRAUMA TO NEONATAL MORTALITY AND INFANT MORBIDITY*

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A factor of outstanding significance in intranatal and neonatal mortality and infant morbidity is the traumatization of the child incident to birth. An increasing appreciation of this source of loss in infants' lives during or soon after delivery is unmistakably expressed in the gradual and steady increase in the number of death certificates that give birth injury as the cause of death. Even so, official vital statistics are still far from disclosing actual conditions. This particular cause of death of the new-born infant only rarely manifests itself conclusively in symptoms and clinical findings, and in the majority of instances can be discovered only by means of an exhaustive postmortem study that includes inspection of the dura folds within the cranium, sectioning of the vertebral column (especially of its cervical portion), and inspection of all abdominal parenchymatous organs with particular attention to the suprarenal glands.

Routine use of this type of extended autopsy reduces to a noteworthy degree that large group of stillbirths and early deaths at present rather generally assigned to asphyxia, prematurity and congenital debility, and also lessens the number of cases in which the customary entirely inadequate autopsy fails to reveal the actual cause of death.

It is impossible to give exact figures as to the frequency with which the child is injured in some way or another in the course of his birth. But the relative importance of birth trauma for intranatal and neonatal mortality is well attested by such facts as the following: In large series of complete autopsies performed subsequent to breech labors and particularly after versions and extractions, the immediate cause of death is found to be of traumatic origin in from 80 to well over 90 per cent. In large series of necropsies done on stillborn infants and

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*Read at the White House Conference for Child Health and Protection, Washington, D. C., Feb. 18, 1931.

*A bibliography pertaining to the facts mentioned in this article may be found in Ehrenfest, H.: Birth Injuries of the Child, ed. 2, New York, D. Appleton & Company, 1931.

those dying within the first few days of life, fatal lesions within the cranium on an average are discovered in about 25 per cent, while in another 25 per cent definite evidence of some damage is present which, however, cannot be positively accepted as responsible for death. The latter group contains many cases in which an edema of the brain or widely distributed minor hemorrhages leave doubt whether they express primary traumatization or represent only secondary phenomena of asphyxia actually induced by interference with fetoplacental blood circulation. It seems likely that about 5 per cent of autopsies on new-born infants reveal a hemorrhage in the suprarenal glands which might have caused death. It is of great practical interest that in severe hepatic injuries sustained in birth (or during brusque efforts at resuscitation), the baby as a rule seems well at first and rather unexpectedly dies on the third or fourth day, and that the cause of death is ascertained only in autopsy.

The cranial structures and parenchymatous organs of the premature baby are particularly vulnerable and, for this reason, are often severely traumatized even in normal spontaneous labor, especially when it progresses rapidly. To a very large extent both the immediate and the later fate of the premature infant is dependent on the degree to which he is traumatized at birth.

It has become evident that failure of a normal onset of the respiratory function immediately after birth in a considerable percentage of cases is due to some damage of the respiratory center. It certainly accrues to the benefit of the new-born infant if the attending physician accepts every deviation from normal in either the infant's respiratory activity or his behavior and actions as suggestive of possible traumatization, which is not necessarily intracranial. This point deserves special emphasis because, with most of the interest lately concentrated on intracranial damage, sight has been lost of the frequent occurrence of other injuries, such as spinal column and cord lesions, hepatic rupture, suprarenal hemorrhages and other accidents that promptly or within a few days lead to death.

Injuries of the infant incident to birth, whatever part of his body they may involve, practically without exception are of a traumatic origin due to various interacting mechanical factors. Their occurrence, however, is greatly influenced and favored by such other conditions as fragility of the bones and blood vessels (prematurity, syphilis), and their consequences are aggravated, for instance, by a lack of ability of extravasated blood to coagulate normally. Under such unfavorable conditions the mechanical forces (especially pressure) at play during every labor might, even in the course of a normal and spontaneous labor, lead to serious damage of the infant. Careful analysis in the individual case, as a rule, will permit acceptable conclusions in regard to the origin of

an excessive force which proved incompatible with the integrity of certain structures. This excess might arise entirely independent of any action on the part of the attending obstetrician as, for example, in a very stormy labor. Most often, however, such damaging compression of the head, shoulders, thorax or abdomen or excessive bending or twisting of the vertebral column will be found to stand in definite connection with intervention of some sort (the administration of an oxytocic, the application of forceps, extraction in breech labor or after version, etc.) or with manipulations incident to resuscitation.

From these and other facts, well founded deductions can be made in regard to the possibility of preventing birth injuries and thus reducing neonatal mortality: Any artificial intervention should be limited to well defined indications and, if possible, should be resorted to only under favorable external conditions. (Forceps extractions made at home will always be more dangerous to both mother and infant than those performed in a hospital.) When interference with labor is decided on solely in the interest of the infant, the selected method of delivery should be practically free from danger to the mother and should not add to the already present risks for the infant. When intervention seems justified in the interest of the mother, the almost inevitably associated risk to the baby should not be disregarded.

While in some instances traumatization of the infant actually cannot be avoided, the incidence and extent of such an accident to a very large degree are determined by the judgment and skill of the obstetrician.

Present information concerning the frequency and variety of birth traumatisms of all kinds leaves no doubt but that it is only a relatively small percentage of cases in which such traumatization proves promptly fatal on account of its severity (fractures of the cranial bones or of the vertebrae, extensive hemorrhages in the skull, spinal canal, abdominal cavity, etc.), as the result of its particular localization (small hemorrhages in the brain, suprarenals, etc.), or under the influence of unfavorable contributory factors (prematurity, hemorrhagic diathesis, etc.). In the majority of instances these injuries are only slight. They may remain unnoticed (abrasions in the mouth, clavicular fractures, slight intracranial damage without hemorrhage, etc.), or the observed effects may disappear quickly and completely (edema of the brain, cephalematoma, facial palsy, etc.). There remains still another large group in which the baby immediately after delivery exhibits such disquieting symptoms as asphyxia or other anomalies of respiration, increased reflex irritability and even convulsions, paralysis of one or more extremities, etc. This group has given rise to the complex question of possible later sequelae and of the significance of birth trauma in later infant and child morbidity. If the aforementioned or similar symptoms persist, one often is finally enabled to arrive at a definite diag-

nosis, such as an intracranial hemorrhage, the central origin of a facial palsy, a serious brachial plexus injury (frequently associated with anomalous respiration as the result of a simultaneous injury to the phrenic nerve), a spinal cord compression by hemorrhage or by a fractured vertebra, fractures of the long bones, and dislocations of the shoulder and other joints, etc. Physical abnormalities noticed early in life commonly are interpreted as congenital while, as a matter of fact, they may be the consequences of injuries sustained in birth.

Reasonable doubt may be entertained whether there exists a direct causative relation, as is claimed by some writers, between intracephalic trauma and spastic vomiting, between minute hemorrhages in the pituitary or suprarenals and deficiencies in later physical growth, between testicular trauma in a breech labor and later azoospermia, or between hemorrhages in the eye or interior ear and later defects of vision or hearing. Certainly in some cases the immediate connection between a birth trauma and a deficiency manifesting itself in later life can be traced. Such a consequent defect is not necessarily of a physical nature. Of the greatest practical interest today is the possible etiologic relation of nonfatal intracranial damage to mental deficiency. It thus can be seen how important it has become from this point of view alone to observe closely the behavior and actions of the new-born infant and to record for later reference even the slightest deviation from normal.

The manifestly exaggerated tendency prevailing during the past decade among pediatricians, neurologists and orthopedic surgeons, of explaining practically all physical and mental deficiencies of younger children on the basis of birth injuries, now has given place to the more reasonable view that such injuries represent the causative factors only in certain cases. In the individual case such an etiologic relation can be established only if precise information is available concerning certain symptoms observed immediately after birth. The mere assertion of the mother or even the ascertained fact that the labor was "long," "difficult," "abnormal" or terminated artificially is insufficient. Neurologists at present seem to agree that in the case of a definite hereditary disposition this factor is more likely to represent the etiologic element. It is more logical to explain the repetition of the same or similar defects in several children of the same mother on the basis of heredity than, as has been done, by an anomaly of the pelvis.

The rôle of the obstetrician in the problem of immediate and delayed consequences of birth traumatization is twofold. In many cases he may prevent the trauma, and he should be able at any time to supply data concerning the new-born that may be indispensable for a correct diagnosis. Prevention of traumatization beyond doubt would reduce

infant mortality during and soon after birth, and would better the chances of the new-born infant for normal development.

Considerable progress has been made of late as the result of more exact information in regard to anatomic and mechanical factors leading to this great variety of possible injuries of the child, and as the result of better knowledge in regard to their possible sequelae.

As far as specific conditions in the United States are concerned, at least two seem to call for serious consideration and correction.

Information concerning fetal and neonatal mortality, as at present furnished by the Bureau of Vital Statistics, does not enable obstetrician or pediatrician to gain precise insight into the relative importance of birth trauma as the actual cause of death. Diagnoses on death certificates such as asphyxiation, congenital debility or prematurity without further qualifications are practically meaningless. It must be admitted that frequently the immediate cause of death can be ascertained only by a thorough autopsy, but it seems likely that more and better information could be secured through appropriate changes in the official birth certificates and death certificates for stillborn or newborn infants. It is hoped that the physicians of this country would not object to the additional work entailed by filling out more elaborate certificates if they be made to understand that additional information given by them will represent one of the most potent aids in the general endeavor of reducing neonatal mortality and infant morbidity rates. (The standard birth certificate gives thirteen reasons for its practical importance, all of a social or economic nature and none mentioning its medical value!)

In view of the unmistakable relation of traumatization of the child to artificial delivery, the rapid growth of an operative trend in the obstetric practice of this country cannot fail to prove alarming. Various reasons for this phenomenon can readily be recognized, some fully justified, others intolerable. But whether the blame rests with physician or patient, it seems that excess in this respect could best be curbed by wide propagation among the women of this country of the fact that ready compliance with their ever-increasing insistence on a short and comfortable labor is not fully compatible with the principles of sane conservative obstetrics and inevitably implies certain risks to themselves and their infants.

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THE PATHOGENESIS AND TREATMENT OF ACUTE OSTEOMYELITIS OF THE JAWS IN NURSLINGS AND IN INFANTS

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The present communication deals with cases of acute osteomyelitis of the jaws—both upper and lower—which occur most commonly in the first few weeks or months of life, and very rarely beyond that period, and which are characterized by: (1) pathologic manifestations associated with the osteomyelitis, which are referable to the mouth, the nose, the nasopharynx and the orbit; (2) the clinical manifestations associated with an acute infection of severe intensity; (3) sequestration and loss of the entire jaw and of the teeth that it customarily carries; (4) the subsequent deformity associated with this loss in the cases in which recovery takes place, and (5) a high mortality.

Similar clinical entities have been described under various names: "gangrenous or sequestrating inflammations of the teeth-pulp of early infancy" (Bronner); maxillary osteomyelitis of infants (Bronner); gangrenous osteogingivitis (Comby, Cozzolino and Bindi); phlegmonous pulpitis (Bronner); sequestrating inflammation of the upper jaw (van Gilse [1]); perialveolar abscess (Moser and S. Kakals); ulceromembranous stomatitis (Gilberti); the stomatitis of Vincent; sequestrierende Zahnkeimentzündung (Zarfl [2]); empyema of the antrum of Highmore in infants (Kelly). The disease of such varied terminology is always described as having a local character; but the confusion that exists concerning the subject is well illustrated by the fact that at times the cases are described as occurring during the course and apparently as a consequence of some general infectious disease, such as measles, whooping cough, etc.; such cases are better dissociated from the group occurring in nurslings and young infants, and are better considered as ordinary cases of hematogenous infection of the upper or the lower jaw.

REVIEW OF THE LITERATURE

An extensive literature has grown up around this subject. The first case of osteomyelitis of the superior maxilla in infants reported

1. van Gilse: Arch. f. Ohren-, Nasen- u. Kehlkopfh. **81**:117, 1928.
2. Zarfl, M.: Ztschr. f. Kinderh. **25**:266, 1920.

in the British literature was by Douglas [3] in 1898. The first case reported in American literature was by Posey [4] of Philadelphia in 1912.

Clinical observations have been made by Moser, S. Kakals (1899), Comby (1904), Kelly [5] (1904), Broca (1904), Movestin (1905), Cozzoloino (1906), Gilberti (1907), Scott-Ridell (1909), Landwerhammer (1909), Fliess (1912), Rocharr (1912), Bindi (1912), Zarfl (1913), J. Francasis (1914), R. Petit (1915) and Landette (1916). The observation is made by many of these that osteomyelitis and necrotic processes of the jaw bones are peculiar to the first year of life. Larger compilations are reported by Neumark [6] (1897), Dependorf [7] (1907), Marx [8] (1922), Kelly (1924), Bronner [9] (1925) and Bass [10] (1928).

ETIOLOGY

Practically all writers are agreed that osteomyelitis of the jaws, just as that of the long bones, must be attributed to bacterial infection. The experience of Allard and Sicard was that in the osteomyelitis of infants and young children pneumococci and streptococci play a much greater and commoner rôle than staphylococci; in older children and in patients of more mature age, the latter organisms are more common in cases of infection of the bone. A coliform bacillus has been a common finding in this group of cases. My own experience is that Staphylococcus aureus is the commonest organism found in osteomyelitis.

The available sources of the infecting organisms are: (1) the vaginal canal of the mother; (2) the fingers of the accoucheur or of the nurse; (3) the nipples and breasts of the mother, and (4) the fingers or apparatus used in cleansing the baby's mouth after birth.

PATHOGENESIS

A minority of the observers have taken it for granted that a general infection must preexist, and that the infection of the jaw is secondary thereto. In proof of this are the cases of Galli (Bacillus coli infection) and of Bass (Staphylococcus aureus infection) in which general blood infection (septicemia) had occurred.

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3. Douglas: Brit. M. J. **1**:368, 1898.

4. Posey, W. C.: Orbital Cellulitis from Disease of the Superior Maxilla in Children, J. A. M. A. **59**:1020 (Sept. 21) 1912.

5. Kelly: Edinburgh M. J. **16**:302, 1904.

6. Neumark, quoted by Galli, P.: Clin. pediat. **8**:604, 1926.

7. Dependorf: Vrtljsschr. f. Zahnh. **26**:195, 1910.

8. Marx, E.: Brit. J. Ophth. **6**:25, 1922.

9. Bronner, H.: Beitr. z. klin. Chir. **133**:163, 1925.

10. Bass, M. H.: Acute Osteomyelitis of the Superior Maxilla in Young Infants, Am. J. Dis. Child. **35**:65 (Jan.) 1928.

The majority of observers have believed that this form of osteomyelitis of the jaws in nurslings and infants is a primary lesion. The various discussions have centered about the method and the point of entry of the organisms into the maxilla and from whence they came.

Most observers who reported on this subject were of the opinion that the alveolar border is the spot where the bacteria enter, because this area of the mouth offers the best opportunity for the invasion of bacteria through small superficial abrasions, and the alveolar process is the most easily wounded spot in the maxilla; the small wounds in the mucous membrane originate in a trauma at birth, or result from the cleansing of the mouth, etc.

Some of the cases have apparently followed infection developing in the mother (Bass, Douglas and Lacasse, Marx, Wood and Dujardin). This is important as showing the origin of the offending organism in certain of the cases.

There is a difference of opinion among various observers who believe in the "primary" nature of this disease as to the part of the jaw—this applies especially to the upper jaw—in which the infection originates and centers and from which it spreads. Opinions vary between the nasal cavity (intrapartum intranasal infection), the antrum of Highmore (Paunz [11]) and the unerupted teeth. Inflammation of the tooth buds in the course of sepsis in the new-born has been described by Swoboda,[12] Zarfl,[2] Finkelstein [13] and von Reuss.[14] Investigators at the Koerner Clinic are of the opinion that the inflammatory process centers chiefly in the tooth anlagen of the canines and milk molars; and with that view the majority of old and new writers on the subject agree.

Proceeding further from these premises, the various observers agree that having once settled in the maxilla the bacteria develop further in the spongiosa of the bone. The process increases progressively just as in osteomyelitis of the long bones; it is followed by suppuration and finally by necrosis and the formation of sequestrums. Although the clinical picture is sharply defined, its diverse manifestations have caused many of the cases to be described as infections of the antrum of Highmore, others as osteomyelitis of the jaw, and others as phlegmons of the orbit. Schmiegelow was the first to show that these cases were in reality cases of osteomyelitis, and Kelly pointed out that the whole superior maxilla is involved, and that evidence of its disease is presented by each of the bony surfaces—the orbital, nasal, facial and palatal.

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11. Paunz: Ztschr. f. Ohrenh. **13**:155, 1925-1926.

12. Swoboda: Ztschr. f. Kinderh. **25**:266, 1920.

13. Finkelstein, H.: Ztschr. f. Kinderh. **25**:266, 1920.

14. von Reuss, A.: Die Krankheiten der Neugeborenen, Berlin, Julius Springer, 1914.

My impression and belief is that osteomyelitis of this type occurring in nurslings and infants is in no way different from the hematogenous form of osteomyelitis in general occurring in other parts and bones of the body, and that the occurrence of the lesion in such young subjects is associated with the physical conditions of childbirth and the environmental conditions immediately following. The localization in the jaws is, as is held by almost everybody, due to various forms of minor or major injury received during childbirth or to various forms of trauma received thereafter associated with the care of the child, especially with the cleansing of the mouth. The predilection for the upper jaw is due to its larger size and to its more rigid construction and attachment in the skull, which favor the more frequent reception of traumatisms. The presence of unerupted teeth and teeth germs or buds determines areas of more marked vascularity which help to determine points of fixation for the metastatic infection. The traumas described as occurring on the alveolar border or elsewhere, which are taken to be the primary points of entry for the infection, should not be assumed to make pathways directly to the bone; these are points of entry pure and simple, and the transmission into the substance of the jaws is made possible only by way of the blood stream and not by simple extension by contiguity.

The mechanism of the pathogenesis and pathology of hematogenous osteomyelitis in general has been discussed extensively on a number of previous occasions, and an extensive discussion of this subject will not be repeated here. Suffice it to say in résumé:

Acute hematogenous osteomyelitis is a metastatic lesion occurring during the course of a bacteremia, the latter resulting from an acute bacterial lesion on a surface of the body which forms the portal of entry for the infection. In this conception a surface of the body includes not only the skin, but also the entire mucous membrane of the alimentary tract, the genito-urinary tract, etc. The common surface lesions include not only furuncles, carbuncles, etc., on the skin, but also easily demonstrable lesions in the tonsils, and in other lymphadenoid collections lying in the mucous membrane of the pharynx, as well as less demonstrable lesions, such as those in Peyer's patches.

The fundamental cause of the spreading of the original lesion in the form of metastatic or subsidiary lesions is an infected thrombus lying in the original area of infection and communicating at some point with the freely circulating blood. Organisms growing on the surfaces of the thrombus are discharged, or pieces of the thrombus itself break off and are discharged into the circulation and, becoming lodged for various reasons in the vascular network of various parts of the body, give rise to secondary lesions. Bone tissue, because of its peculiarities in vascular structure, seems particularly prone to the blocking of these thrombi-

emboli; and the susceptibility to this is particularly increased during the period of growth when the individual bones contain well marked areas at the junction of the diaphysis and the epiphysis, around centers of ossification, around erupting or milk teeth, etc.

The various accessory causes, such as trauma, that determine the localization of a secondary focus of infection—the fixation point—in a given bone are associated with accidents in the local circulation which facilitate blocking of any bacterial thrombus-embolus. The essential nature of the pathologic process that develops at the fixation point is a thrombo-arteritis or thrombophlebitis, and the further development of the process is distinguished by the dominating position that is assumed by secondary vascular thromboses, which must necessarily occur in such a pathologic lesion. The all-important secondary effects that these thromboses produce are disturbances of essential nutrition which lead to the death of certain bone cells and the consequent necrosis of certain areas of bone tissue.

The actual pathogenesis and pathologic process in the jaws are similar to those in other cases of hematogenous osteomyelitis. The point of fixation in the vascular channels of either of the jaws develops into a thrombophlebitis. The occlusion of the vascular channel or channels results in the usual deprivation of blood supply and nourishment, and the amount, degree and character of the resultant necrosis are in direct proportion to the number, size or importance of the vascular channel or channels occluded and the amount of available collateral circulation.

The interesting phase of the blood vessel arrangement [15] for both the superior and the inferior maxilla is found in the dominating fact that the entire blood supply for either bone is derived from one large arterial trunk. The superior maxilla is supplied by the internal maxillary artery, and the branches that form the network of supply are arranged in loops based on the trunk of the internal maxillary artery; each superior maxillary bone is fed by a series of loops which are united in a stem based on the trunk of the internal maxillary artery of its appropriate side. The inferior maxilla is fed by a single vascular loop passing from the internal maxillary artery of one side to that of the other.

This simple anatomic fact explains adequately all the clinical forms of osteomyelitis of the jaws that occur in this group of cases, as follows:

1. Involvement of the entire bone with manifestations referable to the palatal, nasal and orbital surfaces results from a lesion in the stem

15. A much more detailed description of the vascular arrangement of the jaw bones and the rôle of these in acute osteomyelitis of the jaws is contained in another publication on the subject of acute osteomyelitis of the jaws in general (Wilensky, A. O.: Osteomyelitis of the Jaws, Arch. Surg., to be published).

of the internal maxillary artery prior to the giving off of the posterior alveolar branch with or without extension in the loops described, which are derived from the internal maxillary artery. Collateral circulation is at a minimum, and a maximum lesion results.

2. Involvement of the alveolar process results from a lesion in the course of the posterior dental and gingival arteries. The amount of bone involved depends on the amount of collateral circulation.

3. Involvement of the anterior part of the alveolar process and the adjacent part of the bone results from a lesion in the course of the junction of the posterior and anterior dental arteries.

Involvement of the antrum of Highmore occurs with either group 2 or 3. The amount of involvement of the bone depends on the possibilities of collateral circulation.

4. Involvement of the palatal surface results from a lesion in the palatal arteries or may be an extension from an involvement of the alveolar process.

5. Involvement of the nasal aspects of the bone results from a lesion in the nasal and anterior branches of the infra-orbital artery. This variety may also be associated with an empyema of the antrum of Highmore.

6. Involvement of the orbital aspect of the bone results from a lesion in the course of the infra-orbital artery.

The controversy as to whether this form of osteomyelitis of the jaw centers in and is derived from a lesion in the teeth buds, the nose or the antrum or in the neighborhood of the orbit is, to my mind, unnecessary and fruitless as, from the facts outlined, one can easily see that all of these manifestations are simply determined by the dominating position of the thrombophlebitis in the course of the vascular channels described. The seeming importance of any one manifestation is only superficial, and the character of the pathogenesis and pathologic process is, as in other forms of acute osteomyelitis, intimately related to the position of the thrombophlebitis and the resultant necrosis.

GENERAL CLINICAL COURSE

In 82.5 per cent of the cases reported in the literature the first two months of life were involved, the greatest number of the cases falling within the second and third weeks. With few exceptions, the superior maxilla was most frequently diseased. The right and left sides were about equally involved.

The disease presents a clearcut, definite picture, one case report being very much similar to the other. The disease usually befalls healthy infants between 2 and 10 weeks of age, sometimes older ones. The prodromal periods differ; sometimes the children cry and refuse

nourishment, and there may or may not be a slight rise in temperature accompanied at times by diarrhea or constipation; in other cases, the children are violently ill, with high temperatures, vomiting and convulsions.

Then the swelling appears. It may begin in the cheek or in the infra-orbital region, and is almost always accompanied by edema of the lower eyelid. Sometimes there is exophthalmos from edema of the orbit. The sclera is inflamed; conjunctivitis is present, and there is sometimes chemosis. It is these symptoms that usually bring the patient to the ophthalmologist; for instance, three out of four of Nord's patients came from the ophthalmologist. In the majority of cases a localization forms below the inner canthus of the eye. At this site a swelling in the cheek appears, with redness, abscess formation, the breaking through of pus and the formation of a fistula. In the mouth can be noticed swelling of the alveolar process and of the hard palate; this may appear even before the swelling beneath the orbit, and it is, likewise, followed by perforation, the discharge of pus and the formation of a fistula. Presently, numerous small sequestrums discharge through the sinuses. Another common and characteristic symptom is the discharge of premature teeth through the alveolar sinuses. In nearly all cases there is sooner or later a discharge of pus from the nose, which is increased by pressure on the abscess. All of these changes occur within a few days.

The majority of children are really sick, but a few remain surprisingly well in spite of the progress of the disease. The temperature is irregular, convulsions frequently are present, and there are marked anorexia and difficulty in nursing, due to the pus in the nostril. The outcome is either healing, with or without the persistence of discharging sinuses, or the development of secondary purulent foci. Contrary to what one might expect, the prognosis is not always unfavorable. In fatal cases, the infants die as a result of the virulence of the infection before secondary foci have time to develop.

The local manifestations correspond to those in a sequestrum-containing abscess of larger or smaller extent. These accumulations of pus correspond in their pathology to subperiosteal abscesses (such as occur in other locations, especially in the long bones) in relation to the appropriate surface of the maxilla.

Usually, as a final stage a single large abscess cavity exists which harbors the entire, or the major portion of, the necrotic upper jaw; pus is present on all sides in relation to the palatal, alveolar, nasal, orbital and retromaxillary aspects of the jaw. In exceptional instances, owing to the position of the thrombophlebitic lesion and to an extraordinary amount of collateral circulation, the process seems limited to only one aspect of the bone; then either it accumulates in relation

to the upper aspect of the jaw, in which case the manifestations are mainly orbital, or the process seems more limited to the lower aspects of the jaw, and the manifestations appear mostly in the mouth or nose. Frequently the primary accumulation of pus is in the antrum of Highmore; the abscess then usually points primarily in the nose and secondarily in the alveolar process.

In the average case, when a probe is passed into one of the discharging sinuses, it passes at once into a large cavity. This may or may not be a much enlarged antrum cavity; it may be one of the enlarged dental sacs, or it may be a large irregular cavity in which practically the entire superior maxilla is housed as a sequestrum.

SYMPTOMS

Oral Symptoms.—Eighty per cent of the fistulas in the mouth are found at the alveolar arch, of which more than 50 per cent are in the region of the canine tooth. In 60 per cent of the cases an expulsion of the dental pulp occurs. The discharge of teeth and tooth buds through the fistulous openings in the alveolar process is the most characteristic phenomenon of this disease. It leaves the child without teeth over the affected area. The final result, when the child lives, is a considerable deformity of the face and palate with loss of teeth, both temporary and permanent, on the side involved.

Nasal and Antral Symptoms.—A purulent discharge from the nares is a common symptom, and a fistula is present in the nose which leads to bared or necrotic bone.

In an advanced case and, commonly, in early stages of the disease, manifestations referable to the mouth, the nose and the antrum of Highmore appear as a single entity.

Ocular Symptoms.—Of the thirty-five cases tabulated by Marx, ocular symptoms developed in thirty, and Marx was not certain that the remaining five patients did not have them. In eight of the records the ocular symptoms first attracted the attention of the patient's family or of the physician. This is no small percentage, and the ocular symptoms are important because it may happen that the ophthalmologist is the first to be consulted, and the further progress of events may depend on his being able to arrive at a correct diagnosis without unreasonable loss of time. This is not always the case, and examples of this kind are to be found in one of Marx' cases and in a case reported by Dujardin.

The ocular symptoms that appear in osteomyelitis of the superior maxilla can, for simplicity's sake, be divided into those of the eyelids, of the conjunctiva and of the eye socket. The symptoms in the eyelids, according to Brown Kelly, are those that first attract attention to the

process. The swelling, owing to the severe inflammation of the bone, is a severe collateral edema, and is quite easy to understand.

The swelling and redness in the region of the lacrimal sac and the subsequent fistula are frequent symptoms. They are important because they may also easily lead to an incorrect diagnosis. According to Brown Kelly, an abscess often forms in the lower eyelid, and pus exudes apparently from the lacrimal sac. The fistula just at this point is to be explained by the fact that the inflammation often overdevelops in the nasal process of the superior maxilla, and the pus collects there, eventually seeking the easiest method of exit, which in this case leads to the inner corner of the eye. The canaliculi remain untouched; it is well to remember this, because one might be too zealous and, to the patient's detriment, begin an active treatment of the canaliculi if one did not pay proper attention to the other symptoms. Marx advised one to be as conservative as possible, and even in the commencement of abscess formation in the lower eyelid to make no incision in the abscess, as frequently treatment via the palate and processus alveolaris will effect a complete cure, while an ugly drawn scar with ectropion may result from incision, as appears from the report of Avellis.

The conjunctivitis, like the swelling of the eyelids, is usually part of a collateral edema. The degree of severity of the original infection can thereby appear to a certain extent from the chemosis.

Exophthalmos was observed by Marx in ten of the thirty-five cases. In comparison with the other ocular symptoms, this occurs too seldom to be regarded as an expected phenomenon. Exophthalmos is also an accompaniment of inflammation of the ethmoid. Stephenson reported ten cases of inflammation of the ethmoid, which showed exophthalmos to a greater or lesser degree. Thus it appears that the protrusion of the eye is attendant on the inflammation of the bony walls of the orbit fossae, which is followed by purulent exudation in the eye socket.

It is surprising that in the ophthalmic literature practically nothing is to be found about the ocular complication of osteomyelitis of the upper jaw. There is one reference by Eversbusch[16] in which he pointed out the possibility of mistaking a fistulous osteomyelitis of the superior maxilla for a discharging lacrimal duct.

DIFFERENTIAL DIAGNOSIS

A differential diagnosis must be made from the following conditions:

1. Ophthalmia neonatorum. Usually both eyes are affected, and gonococci can usually be found. Furthermore, the edema does not extend to the infra-orbital region, nor to the alveolar process.

16. Eversbusch: Die Augenerkrankungen im Kindesalter.

2. Erysipelas.
3. Dacryocystitis.
4. Syphilis and tuberculosis. Usually the anamnesis and general examination will point to the diagnosis.

Careful examination of the patient, together with the requisite laboratory work in association with a carefully taken history, should result in a correct diagnosis. In addition, the characteristic phenomenon of exfoliation of teeth or tooth buds should by itself suffice to call one's attention to the correct condition.

BLOOD CULTURES

One of Bass' patients had Staphylococcus aureus in the blood. The literature otherwise does not contain any specific statements in regard to this aspect of the disease. I feel sure, however, that cultivations of the blood behave no differently in osteomyelitis of the jaws than they do in osteomyelitis of other bones; Bass' case is a confirmation of this statement.

TREATMENT

The general principles governing the treatment for acute osteomyelitis have been fully described on several previous occasions and will not be repeated here. Suffice it to say that in nurslings and in infants osteomyelitis of the jaws should be divided into the following two groups:

1. A group consisting of the cases that terminate fatally as a result of the profound toxemia that develops. The fatalities usually occur in early stages of the disease, and whatever one does in the way of treatment is mostly of a temporizing and palliative nature and shows no influence on the progression of the local and general phenomena of the disease.

2. This group contains the remainder of the cases. It is most important to be as conservative as possible. In the early stages, careful cleansing of the mouth, possibly poulticing in appropriate cases, and conservative attention to the nasal and orbital manifestations are all that is required. As soon as definite areas of fluctuation are discovered, these should be adequately but conservatively incised with due attention to the placing of the incisions. As much as possible should be done from the interior of the mouth and through the nasal cavities. It is surprising how one can reach foci of suppuration at apparently distant points from the buccal cavity, especially in the interval between the cheek and the bone, particularly in the canine fossa; this is possibly due to the general involvement of the entire bone in the process. Marx has been able adequately to drain orbital abscesses

from appropriately placed incisions in the mouth. There is no record available of any permanent effect on the eye itself or on sight.

As sequestration is common, one should assist nature as well as one can in enabling these necrotic fragments to be discharged. The teeth usually are discharged from the fistulas in the alveolar process; the major portion of the bone itself usually comes away through an opening in the fold between the cheek and the bone.

Abscesses in association with the lower jaw are more simple technically, and one should follow ordinary surgical principles in treating them. Sequestrums should not be removed until involucrum formation is abundant.

EARLY MENTION OF A HARLEQUIN FETUS IN AMERICA

J. I. WARING, M.D.
CHARLESTON, S. C.

In a diary kept by the Rev. Oliver Hart, A.M., pastor of the Baptist church in Charleston, S. C., in colonial times, the following entry is found:[1]

On Thursday, April ye 5th, 1750, I went to see a most deplorable object of a child, born the night before, of one Mary Evans, in Chas: town. It was surprising to all who beheld it, and I scarcely know how to describe it. The skin was dry and hard, and seemed to be cracked in many places, somewhat resembling the Scales of a Fish. The Mouth was large and round, and wide open. It had no external nose, but two Holes where the Nose would have been. The Eyes appeared to be lumps of coagulated Blood, turned out, about the Bigness of a Plumb, ghastly to behold. It had no external Ears, but holes where the Ears should be. The Hands and Feet Appeared to be swoln, were crumpt up, & felt quite hard. The back part of its Head was much open. It made a strange kind of a noise, very low, which I cannot describe. It lived about eight and forty hours, and was alive when I saw it.

1. The diary is printed in the Year Book of the City of Charleston, S. C., for 1896.

Pediatric Biographies

LUIGI TANSILLO

About 1510—About 1569

JOHN RUHRÄH, M.D.
BALTIMORE

Soldier and poet, Tansillo must claim the attention of the pediatrician, for he wrote a most interesting poem on the subject of nursing. He was born in Nola, a town of the Kingdom of Naples, about 1510, and it is stated that he came from a distinguished family, whose good name he perpetuated by his prowess in arms and his skill in poetry. Torquato Tasso mentions him in his dialogue "Il Gonzago," and he is one of the few to whom Tasso gave the appellation "leggradro" or elegant.

He wrote lyrics, a pastoral comedy, a poem entitled "Il Vindemniatore," "Il Podere," which gives directions for choosing a country seat, and a lengthy one called "Le Làgrime de San Pietro" (The Tears of St. Peter).

"Il Vindemniatore" was witty, but a little too lacivious for the authorities, and Pope Pius IV put it in the Index Expurgatorius, but an apology in the shape of an ode addressed to the Holy Father put him in the good graces of the Vatican and his name was omitted from the next list.

"La Balia," or in English "The Nurse," was written against the abuses practiced by the gentry of the time in neglecting their infants and employing wetnurses, but for some reason it was not published until about two centuries later when, in 1767, Giovan Antonio Ranza found a manuscript copy which he published with copious notes.

Tansillo evidently knew medicine as it appeared in Celsus, Galen and other classic writers. Some of his ideas, as the translator notes, were borrowed from the "Noctes Atticae" of Aulus Gellius.

In 1798, a translation into English by William Roscoe was published, and a reprint appeared in New York in 1800. The translator says that "the subject is in a high degree interesting, and is treated in a manner peculiarly pointed and direct, yet without violating that decorum which is due the public at large, and particularly the sex to whom it is addressed."

Among other things he rails against the pampering of pets by women, a vice of all ages.

THE

NURSE,

A

POEM.

TRANSLATED FROM THE ITALIAN

OF

LUIGI TANSILLO.

BY WILLIAM ROSCOE.

LIVERPOOL,
PRINTED BY J. M'CREERY,
FOR CADELL AND DAVIES, STRAND,
LONDON.
1798.

Title page of the English translation of "La Balia."

What fears ye feel as slow ye take your way
Lest from your path the minion chance to stray,
At home on cushions pillowed deep he lies.

* * * * * * *

Whilst your young babe that from its mother's side
No threats should sever and no force divide
In hapless hour is banished far aloof
Not only from your breast, but from your roof.

He comments on maternal nursing and warns of wetnurses, but if one must use them he gives directions for their choice.

A few lines will give a general idea of the style of the translator.

Once exil'd from your breast, and doom'd to bring
His daily nurture from a stranger spring,
Ah who can tell the dangers that await,
Your infant, thus abandoned to his fate?
Say, is there one with human feelings fraught
Can bear to think, nor sicken at the thought,
That whilst her babe, with unpolluted lips,
As nature asks, the vital fountain sips;
While yet its pure and sainted shrine within
Rests the young mind, unconscious of a sin,
He with his daily nutriment should drain,
That dread disease which fires the wanton's vein;
Sent as the fiercest messenger of God,
O'er lawless love to wave his scorpion rod?

Strange is the tale, but not more strange than true,
And many a parent may the treachery rue,
Who for their child, neglected and unknown,
Receive a changeling, vainly deem'd their own.

The original is in easy flowing style, and just a bit of introduction is not out of place here:

D'Orfeo vorrei, che fosse ora il dir mio,
Non perchè l'alma oppressa si rileve;
Ma per darvi a veder quel, ch' io desio.

Pur, se 'l vero ha la forza, ch' aver deve
Negli animi gentili, come'l vostro,
Darlo a creder a voi mi serà lieve.

Ne per desiò d' onor verso l' inchiostro,
Ma per un zelo santo, e naturale,
Che mi muove à pietà dell' error nostro;

E so, che l' emendar d' un sì gran male,
O Donne, è in mano a voi, qualor vogliate;
Se d' adoprar virtù punto vi cale.

(I wish that Orpheus would arouse me not that the oppressed soul would rise but to make you see what I desire. For if the trust has the force it should have in a gentle soul like yours it will be easy for me to make you believe me. Not for desire of honor do I dip this ink but by a holy and a natural zeal which moves me to the pity of our error. And I know that to correct so great an ill, O Ladies, is in your hand whenever you will, if you care to make a virtue of this point.)

Pediatrics in Art

HORUS

JOHN RUHRÄH, M.D.
BALTIMORE

Isis, identified with the Greek Ceres, was the goddess of medicine, marriage, fecundity and maternity. She was the daughter of Nut, or the sky, the wife of Osiris and the mother of Horus. Set, the god of evil and the brother of Osiris, conspired against the latter, who was king of Egypt. Osiris was put in a chest, thrown into the Nile and carried to the seashore where after a long search he was found by Isis, who hid him while she went to urge Horus to avenge his father. Meanwhile Set found the body and cut it into fourteen pieces scattering them over Egypt. Isis then traveled about building temples over each piece of the body where she found it. Osiris became the lord of the other world and taught Horus the use of arms. Horus defeated Set and took him prisoner, but Isis freed him. This so enraged Horus that he cut off his mother's head, but Thoth replaced it with the head of a cow. The outstretched wings of Isis are frequently seen in Egyptian decorations. She is often represented with the face of a woman and the horns of a cow, sometimes with the lotus on her head and at other times hooded. Isis worship spread from Egypt to Greece, Rome, Gaul and Britain and continued to the reign of Justinian.

Horus was the sun god and identified with Apollo. He is sometimes represented seated on a lotus flower with his finger in his mouth as a symbol of secrecy or silence.

The illustration to the left is a statue of Isis nursing Horus. This is in the Louvre, in Paris. (Photograph by Giraudon.)

To the right is a small figure of the same subject, now in the collection of Dr. T. G. H. Drake, of Toronto, through whose courtesy it is reproduced.

Isis Nursing Horus

News and Comment

UNIVERSITY NEWS

The chair in the Graduate School of Medicine of the University of Chicago, originally endowed in 1916 by C. R. Crane and R. T. Crane, Jr., in memory of their father, Richard T. Crane, founder of Crane Company, has been assigned to the Department of Pediatrics, and Dr. Frederick W. Schlutz, professor and chairman of the Department of Pediatrics, has been appointed as the first Richard T. Crane professor of pediatrics.

Dr. L. E. Leenhardt has been promoted to professor of the pediatric clinic of the faculty of the University of Montpellier.

SOCIETY NEWS

North Carolina Pediatric Society.—A group of North Carolina pediatricians in Durham have organized the North Carolina Pediatric Society. The officers are: Dr. Yates W. Faison, Charlotte, president; Dr. Thomas M. Watson, Greenville, vice president, and Dr. Ewen K. McLean, Charlotte, secretary.

GENERAL

New Pediatric Unit in St. Louis.—A pediatric division with beds for forty children and eight infants was opened in St. Mary's Hospital, St. Louis, in December. This will become the pediatric teaching unit for St. Louis University School of Medicine.

Institute of Child Guidance to Be Discontinued in New York.—Financial support of the Institute for Child Guidance, established five years ago by the Commonwealth Fund as a training center for psychiatric work, will be withdrawn by the Fund on July 1, 1933.

DEATHS

We regret to report the death of Dr. Alegandro Infante, of San Diego, Chile, and Dr. Eugene Revilliod of Geneva, Switzerland.

PERSONAL

Dr. Frederick W. Schlutz was the guest of honor at a luncheon and a dinner given by the Cuban Academy of Science and the Havana Pediatric Society in Havana on November 17. He addressed these societies on the subject of "The Importance of Vitamins in Child Nutrition."

Correspondence

"VIOSTEROL AND COD LIVER OIL: COMPARATIVE OBSERVATIONS"

To the Editor:—The article of Prather, Nelson and Bliss on viosterol and cod liver oil, which appeared in the July issue of the AMERICAN JOURNAL OF DISEASES OF CHILDREN, page 52, prompts me to make the following comment with the hope of correcting an erroneous impression that the article conveyed in regard to the clinical and experimental use of viosterol. Proof of this misunderstanding may be seen in the recent advertising matter of the E. L. Patch Company and the various abstract journals that copy only the author's conclusions.

The authors of this article infer that the manufacturers of viosterol are vague about their product. This, they state, has misled the laity and the medical profession in thinking that viosterol is "a concentrated substitute for cod liver oil." In justice to the manufacturers, it must be said that their advertising and labeling of this product is in no way misleading. On the contrary, each bottle is labeled plainly "Viosterol, 250 D" without mention of its being a substitute or identical with cod liver oil. Their advertising matter frequently contains mention that "unlike vitamin D which is relatively scarce in common foodstuffs, vitamin A (contained in cod liver oil) is fortunately abundant in the daily diet — butter, milk, eggs, and a dozen vegetables all afford vitamin A in liberal amounts" (from *J. A. M. A.*, July 11, 1931, vol. 97). With such a plain statement in an advertisement of viosterol in regard to the difference between viosterol and cod liver oil and with the constant stressing of this difference by advertisements of cod liver oil, there should be no fear "that there is a growing belief among pediatricians and physicians in general that viosterol is a concentrated substitute for cod liver oil." Most physicians and nutrition workers are quite aware of the specific functions of vitamins A and D, and that they are not interchangeable. At least they know that since the epoch-making experiments of McCollum, Simmonds, Shipley and Park (*J. Biol. Chem.* **50**:5, 1922; **53**:293, 1922), it would be quite unwise to attempt to cure rickets with vitamin A or xerophthalmia with vitamin D — a feat attempted by Prather, Nelson and Bliss.

Aside from the attempt to cure xerophthalmia with vitamin D, the authors' conclusions are not warranted by their experimental results. Their assertion that "the substitution of viosterol for cod liver oil in the diet is not logical and may result in an appreciable decrease of the child's strength and resistance to infection" is highly exaggerated and has no experimental or clinical basis. From my own experience with viosterol in more than 1,000 controlled cases and from the experiences of others, I know of no case of xerophthalmia which developed during viosterol therapy. Moreover, the incidence of xerophthalmia is exceedingly rare in the United States, even in children who suffer from the most severe types of rickets brought about by poor dietaries. Evidently vitamin A is so widespread that the child receiving the poorest sort of a diet probably receives an adequate amount of this vitamin. In our series on viosterol the incidence of infections of the upper respiratory tract was not greater than in any other group of children. In many cases the administration of a larger dose of vitamin D in the form of viosterol cured the rachitic deformities of the chest in a much shorter time than would have been possible with cod liver oil, and thereby the occurrence of infections of the lungs may have been warded off.

While I do not question the beneficial results from the use of a properly standardized cod liver oil, yet I believe that in many instances viosterol is superior. This is especially true in tetany, and in very severe rickets, late rickets and celiac disease. The choice of the use of either depends on many factors and should be left to the discretion of the physician, who should be informed through controlled experimentation rather than through misleading abstract literature which he receives in his daily mail.

DAVID H. SHELLING, M.D., Baltimore.

To the Editor:—Several days ago Mr. Prather handed me your letter of Nov. 20, 1931, and the copy of Dr. Shelling's communication. Please accept our thanks for sending the material. Following you will find our comments:

In reply to the statements of our friendly critic, Dr. David H. Shelling, who is filling a Mead Johnson & Company grant at the Harriet Lane Home for Invalid Children at Baltimore, we wish to state first that all of the materials used were provided by manufacturers who were fully acquainted with our plans, who expressed approval and appreciation of the work, and who indicated, after the presentation of the paper, that modifications of their printed matter would undoubtedly follow, to avoid the possibility that readers might misconstrue printed statements. We think that this commendable attitude is common to all manufacturers of legitimate medicinal articles.

Dr. Shelling is in error when he states that we "inferred" that manufacturers' (please note that we said "some" manufacturers') statements were being misconstrued by some members of the medical profession and by the laity. Our attention was first called to the situation by two pediatricians of reputation and long experience. We then interviewed many physicians, dentists, pharmacists, nurses and members of the laity, and found that the situation was even more grave than they had thought; i. e., that there is a growing belief that viosterol is a concentrated, complete substitute for cod liver oil, and that viosterol is enjoying an increasing popularity as a complete "substitute" for cod liver oil. We agree that "most physicians and nutrition workers are quite aware of the specific functions of vitamins A and D and that they are not interchangeable." Our statement is: "Although aware of the fact that cod liver oil contains two vitamins and viosterol only one, the average physician is better acquainted with the antirachitic vitamin, and is likely to disregard the importance of fat-soluble vitamin A and its influence on the child's resistance to infections."

Dr. Shelling has not seen, apparently, packages of the product such as we have on our desk, for he states that "each bottle is labeled plainly 'Viosterol, 250 D' without mention of its being a substitute or identical with cod liver oil." Purely in the interests of accuracy we wish to state that attention was called to the statements of some manufacturers which were being misconstrued by some readers. We did not say that the manufacturers were deliberately stating that viosterol is a substitute for, or identical with, cod liver oil; neither did we suggest that they were intentionally vague or indirect in their statements. Dr. Shelling is quoting from packages that made their appearance after the presentation of the paper at the Memphis meeting of the Central States Pediatric Society. Soon after the Memphis meeting certain changes, forecast by some manufacturers' representatives, were made on the labels of some brands of viosterol. We have before us several packages of the product which were provided by the manufacturers before and during our experimental work. One of these packages bears the statement "Standardized Potency 100 Times the Vitamin D Value of Cod Liver Oil." Inside these packages we find a slip that is intended not for the physician or dentist,

but for members of the laity, for it begins with the statement "Your baby's feeding problems are different from those of other babies and in fact vary at different times. Your physician is the only qualified advisor in these matters which vitally affect your baby's health and future, etc." Of course, it may be argued that "here is proof" that the product is to be prescribed only by the physician, and we agree that only the physician should prescribe drugs. However, it appears that the mere inclusion of such slips is proof that it was recognized that the package would probably be sold directly to the laity, and the interpretation of the "literature" thus left to them. We find also the statement on this package that the product "is a tasteless preparation of Vitamin D, two drops corresponding in Vitamin D potency to approximately one teaspoonful of good Cod Liver Oil. It may be taken directly by mouth or with any item of the infant or adult diet, etc." Another package bears the statement "Antirachitic (Vitamin D) potency 100 times that of standard antirachitic Cod Liver Oil." "Two drops (⅔ minim) of Viosterol equal in Vitamin D Potency one teaspoonful (1¼ dram) of standard antirachitic Cod Liver Oil." "Viosterol is tasteless and does not interfere with the appetite or digestion." In comparing the foregoing statements with a new package, we find the labeling simply "Viosterol (activated Ergosterol) in Oil—250 D," as quoted by Dr. Shelling; no doses are suggested. However, the "Your baby" slip is inclosed. In view of these facts we think that the manufacturers recognized the truth of our statements, and that some of them, at any rate, have corrected their literature accordingly. The persons whom we interviewed and who were of the impression that viosterol was acceptable as a complete substitute for cod liver oil stated that they received this impression from the statements on manufacturers' packages and in manufacturers' literature, or that this information had been given them by physicians, dentists, pharmacists or nurses. Kindly note the "250 D" on the newer package in the light of our experimental work.

We have not seen the recent advertising matter of the E. L. Patch Company, and we regret that Dr. Shelling has seen only an abstract of our article. We will send a copy of the complete paper to him. Dr. Shelling will find that our bibliography includes the epoch-making experiments of McCollum and his co-workers, together with fifty-two additional references to the literature.

Dr. Shelling probably made his "a feat attempted by Prather, Nelson and Bliss" statement in a facetious fashion. His difference of opinion in the matter of our conclusions we think is purely a matter of difference of opinion and interpretation. In the light of our experimental work, we reiterate our fifth conclusion, together with the other four. The suggestion brought out in our fifth conclusion agrees with the opinions expressed by a number of pediatricians of long experience and ability who collaborated with us. We are looking forward with great interest to the report of the more than 1,000 controlled cases of Dr. Shelling. Dr. Shelling has properly qualified his "Viosterol superior" statement. The striking potential opportunities for misconstruction that may be drawn from Dr. Shelling's sentence "While I do not question the beneficial results from the use of a properly standardized cod liver oil, yet I believe that in many instances viosterol is superior," if isolated, are obvious. We agree with Dr. Shelling that the choice of therapeutic measures should be left to the discretion of the attending physician, who should be informed and thoroughly acquainted with the properties, actions and uses of the agents he is utilizing. (See the advertisement on the inside front cover of the *American Review of Tuberculosis*, November, 1929, vol. 20; also *Archives of Pediatrics* **48**:i [March, July and Nov.] 1931.)

A. R. Bliss, Jr., Memphis, Tenn.

Abstracts from Current Literature

Pathology, Bacteriology and Biochemistry

THE EFFECT OF ATELECTASIS ON THE PULMONARY BLOOD VOLUME. JACOB FINE and CECIL K. DRINKER, Arch. Surg. **22**:495 (March) 1931.

Experiments were carried out on rabbits to determine the normal ratio of total blood volume of the two lungs and to observe the effect of a partial or complete compression atelectasis (pneumothorax) and also of a total obstruction atelectasis (bronchial ligation) on the ratio. Experiments showed that complete atelectasis induced by pneumothorax at once reduces the total blood volume of the affected lung by amounts varying, on an average, between 25.9 and 54.5 per cent. Absorptive atelectasis reduces the total blood volume of the affected lung by 46.9 per cent. The author outlines a reliable chemical method for the quantification of the relative blood volumes of the two lungs in the rabbit.

KAISER, Rochester, N.Y.

EXPERIMENTAL SHOCK: OBSERVATIONS ON THE WATER CONTENT OF THE TISSUES OF THE BODY AFTER TRAUMA AND AFTER HEMORRHAGE. P. N. HARRIS and ALFRED BLALOCK, Arch. Surg. **22**:638 (April) 1931.

Experiments on the study of shock by the authors showed that the fluid that escapes from the blood stream at the site of injury after mild trauma to an extremity, after trauma to the intestines and after burns has approximately the same composition as the plasma of the blood. Dogs anesthetized by barbital were traumatized while the control dogs were also anesthetized. The content in water and solids of various tissues of the body was determined. There was little difference in the content in water or solids of the tissues in the two groups. In other experiments the content in water and solids of the blood and tissues was determined before and after a low blood pressure had been produced by the removal of whole blood, blood plasma or by mild trauma to an extremity. The results were compared with those obtained in experiments in which the animals were simply given barbital and left on the table for periods of time varying from twenty-six to forty-seven hours. It was found that there was a larger loss of water by the muscles in control experiments than in those in which hemorrhage or injury was studied. Reasons are given for the belief that hemorrhage and trauma are similar in that in each there is a loss of plasma proteins with a diminution in the total osmotic pressure.

KAISER, Rochester, N. Y.

THE ABSORPTION OF DEXTROSE FROM THE COLON. R. W. MCNEALY and J. DANIEL WILLEMS, Arch. Surg. **22**:649 (April) 1931.

Based on experiments on dogs, the authors found that a 5 per cent solution of dextrose is not absorbed from the colon to any appreciable extent, while tap water and physiologic solution of sodium chloride are rapidly and efficiently absorbed. Dextrose was given, with a mixture of some other chemical. When given with sodium chloride a small amount of dextrose was absorbed from the colon, but there was no appreciable absorption from a dextrose-sodium bicarbonate mixture. There was no absorption when a dextrose-alcohol mixture was injected. The authors conclude that there is no evidence to show that the dextrose enema is of any practical nutritional value.

KAISER, Rochester, N. Y.

THE DIMENSIONS AND GROWTH OF THE PALATE IN THE NORMAL INFANT AND IN THE INFANT WITH GROSS MALDEVELOPMENT OF THE UPPER LIP AND PALATE. WILLIAM T. PEYTON, Arch. Surg. **22**:704 (May) 1931.

A difference of opinion as to whether there is a deficiency of tissue in cases of congenital clefts of the upper part of the face and jaw inspired the author to collect data on general body and head measurements and palate measurements. Measurements were taken on malformed children and normal children of the same age and size. The fronto-occipital diameter of the normal children was compared with the same dimensions of the maldeveloped children. There was no significant difference in the fronto-occipital diameter in these two groups. The size of the head is therefore approximately the same for normal as for maldeveloped children. When the surface width of the normal palate was compared with that of the cleft palate it was found that the fitted line of trend for the maldeveloped material for 51 cm. in length was approximately 1.3 mm. less than for the normal material, and for 59 cm. in length it was 1 mm. less. The transverse diameter of the cleft palate is greater than the transverse diameter of the palate of the normal child of equal body length. The difference in width at lengths of 51 and 59 cm. is approximately 7 and 5 mm., respectively. For a crown-heel length of 51 cm. the height of the palate is approximately 3 mm. more, and at 59 cm. length, 2.5 mm. more. The length of the alveolar process in the maldeveloped children was slightly above that in normal children. Utilizing all measurements, it was found that the dimensions of cleft palate, except for surface width, are larger than those of the normal palate.

KAISER, Rochester, N. Y.

THE OCCURRENCE OF DIPHTHEROIDS IN ROUTINE BLOOD CULTURES. LUTHER THOMPSON, J. Bact. **21**:45 (Jan.) 1931.

Immediately on withdrawing the blood from the patient, 2 cc. is added to 30 cc. of dextrose brain broth in a 1 by 7 inch tube. At the end of fourteen days, or sooner if growth is apparent, a Gram stain is made, and 0.1 cc. of the sediment is inoculated in a tube of soft brain agar (0.3 per cent agar) in five-eighths by 8 inch tubes. These are, in turn, incubated for fourteen days unless growth appears earlier. Approximately 600 cultures have been studied. Diphtheroids have not been observed to appear in cultures before the third or fourth day in this series. Between 2 and 3 per cent of all cultures negative after two days have later shown a growth of diphtheroids.

STOESSER, Minneapolis.

PROMOTION OF PHAGOCYTOSIS BY CALCIUM GLUCONATE, SODIUM IODIDE, DEXTROSE AND OTHER SUBSTANCES. RUTH TUNNICLIFF, J. Infect. Dis. **48**:161 (Feb.) 1931.

This worker investigated the phagocytic stimulating power of various agents and found that solutions of calcium gluconate, calcium chloride, sodium salicylate, sodium iodide and neoarsphenamine caused increased phagocytosis while physiologic solutions of salt, distilled water, milk, sodium phosphate or mercurochrome-220 soluble in water or in dextrose caused no increased phagocytosis. An increase was best noted with an intravenous injection at least twenty-four hours earlier than with an intramuscular injection. Some increase was noted when calcium gluconate was given by mouth.

TOOMEY, Cleveland.

CUTANEOUS HYPERSENSITIVENESS IN GUINEA-PIGS INFECTED WITH BRUCELLA ABORTUS. AXEL C. S. STROEM, J. Infect. Dis. **48**:167 (Feb.) 1931.

There is a great deal of interest as to whether or not cutaneous hypersensitivity is evidence of disease, either past or present. The author worked with *Bacillus abortus*. He found that heat-killed vaccine of *B. abortus* or mixtures of vaccine and

kieselguhr when injected into guinea-pigs did not create a cutaneous hypersensitivity to abortin. His further experiments illustrated the specificity of various strains of *Brucella*. He showed that guinea-pigs given injections of *B. abortus* gave negative tuberculin reactions.

TOOMEY, Cleveland.

THERAPEUTIC ANTIMENINGOCOCCUS SERUMS: THEIR NEUTRALIZING POTENCY AS MEASURED BY THE PHENOMENON OF LOCAL SKIN REACTIVITY. GREGORY SHWARTZMAN, J. Infect. Dis. **48**:339 (April) 1931.

Shwartzman draws attention to the fact that many antimeningococcus serums are poor in neutralizing antibodies as tested by the Shwartzman phenomenon. Using the same guide, he concluded that Banzhaf's method of antimeningococcus serum concentration is effective. He feels that active immunization in horses should be carried out by injections of toxic filtrates as well as by live cultures.

TOOMEY, Cleveland.

LOCAL SKIN REACTIVITY TO "FILTRATES" OF PNEUMOCOCCUS. ELIZABETH J. COPE and KATHARINE M. HOWELL, J. Infect. Dis. **48**:570 (June) 1931.

These authors thought that Shwartzman's phenomenon could be used to determine type specificity more accurately than agglutination. They regard their preliminary tests as inconclusive. Incidentally they found that a pneumococcal toxic substance was obtained by dissolving pneumococci in bile.

TOOMEY, Cleveland.

SIMULTANEOUS MULTIPLE IMMUNIZATION. LUDVIG HEKTOEN and ALDEN K. BOOR, J. Infect. Dis. **48**:588 (June) 1931.

These workers showed that the rabbit could be given simultaneous injections of various totally unrelated antigens with the subsequent development of specific precipitins. In one instance, thirty-five antigens were used and thirty-four specific precipitins developed.

TOOMEY, Cleveland.

INVESTIGATION ON THE PRODUCTS OBTAINED BY EXPOSING OILS AND CARBOHYDRATES TO SUNLIGHT IN PRESENCE OF AIR. SACHINDRA NATH CHACRABARTI and N. R. DHAR, Indian J. M. Research **17**:430, 1929.

If olive, mustard, coconut, mahwa, castor, sesame and linseed oils, butter and some carbohydrates are exposed to sunlight and air is passed through them, peroxides are formed. In the absence of air, the amount of peroxides is decreased. All these oil peroxides have the property of oxidizing a solution of dextrose at 40 degrees for eighteen hours. From experiments on the metabolism of pigeons, using exposed and unexposed oils, iron and sunlight, it was proved that sunlight is the best preventive of polyneuritis and beriberi; olive oil exposed to sunlight is next best, whereas iron and unexposed oils are harmful.

KUGELMASS, New York.

A NEW COLOR REACTION FOR ERGOSTEROL: THE DIFFERENTIATION OF IRRADIATED AND NONIRRADIATED ERGOSTEROL. R. MEESEMAEKER, Compt. rend. Acad. d. sc. **190**:216 (Jan. 20) 1930.

The Liebermann test for sterols can be modified to give a specific color reaction for ergosterol through replacement of the concentrated sulphuric acid with anhydrous zinc chloride. The color produced is red, followed by a green which is quite stable. A solution that has been exposed to irradiation under a mercury vapor light gives a final green solution the intensity of which is proportional to the radiation.

KUGELMASS, New York.

THE BASAL METABOLISM OF HYPOPHYSECTOMIZED DOGS. ARGENTINA ARTUNDO, Rev. Soc. argent. de biol. **6**:497 (Nov.) 1930.

A study was made of the basal rate in dogs in which the hypophysis had been removed. The author was able to demonstrate a decrease in the basal metabolism of five of the eight dogs operated on. The average fall was 15.8 per cent for the eight dogs, varying from 0 to —32 per cent. The average per square meter was 666 calories in the dogs operated on and 795 calories in the five controls. The respiratory quotient was the same in the two groups.

HARRISON, Iowa City.

THE EFFECT OF ULTRAVIOLET RAYS ON BLOOD ENZYMES. B. M. KOLDAYEV and M. M. ALTSCHULLER, Ztschr. f. physiol. Chem. **186**:223, 1930.

A single exposure of gray rabbits for from ten to sixty minutes to a 1,500 chemically pure mercury-silicon dioxide lamp at a distance of from 50 to 100 cm. resulted in a temporary decrease in amylase and blood catalase and an increase in serum lipase. However, the decrease in amylase was not observed in all the animals. The extent of alteration in enzyme content showed no direct relationship to the intensity of irradiation as determined by the time of exposure and the distance from the lamp. With repeated exposures the changes in enzyme content were essentially the same. Here there was a gradual increase in lipase and a decrease in catalase, and in some cases a gradual decrease in amylase.

KUGELMASS, New York.

INFLUENCE OF VEGETABLE CATHARTICS ON EPINEPHRINE HYPERGLYCEMIA. O. TAKASHINA, J. Pediat. (Tokyo), March 20, 1931, no. 370, p. 377.

The author administered castor oil, croton oil and telepine oil into the stomach by an enteric fistula in dogs, in order to study the absorption phenomenon through the gastro-intestinal mucosa, by observing the degree of hyperglycemia induced by epinephrine (from 0.5 to 0.66 cc. per kilogram). Of these three cathartics, castor oil showed no influence in the absorption of epinephrine; croton oil showed the greatest influence, while telepine oil occupied an intermediate position. The greater the degree of inflammation of the mucosa and the younger the animals, the greater was the absorption of epinephrine. This applies to the absorption phenomenon in acute enteritis and diarrheas in infants, in which there is a constant absorption of abnormal materials from the intestinal walls. In administering the cathartics, then, this possible effect on the permeability of the intestines should be remembered.

KATO, Chicago.

Nutrition

COD-LIVER OIL AND THE VITAMINS IN RELATION TO BONE GROWTH AND RICKETS. H. A. HARRIS, Am. J. M. Sc. **181**:453 (April) 1931.

An excellent hour's reading is presented in this article, which received the Alvarenga prize of the College of Physicians of Philadelphia in 1930. A summary of the history of the therapeutic uses of cod liver oil, with special reference to rickets, is given, as well as some pertinent remarks concerning vitamin therapy and the present status of bone chemistry and formation. From the attendant discussion one vital fact is revealed; namely, that cod liver oil still remains the most dependable and most valuable aid in the treatment for rickets.

HENSKE, Omaha.

INTRAPERITONEAL INJECTION OF DEXTROSE. M. ACUNA and S. I. BETTONOTTI, Rev. de especialid. **6**:14 (May) 1931.

The authors have used intraperitoneal injections of isotonic dextrose with success. This treatment is indicated in all cases of dehydration and dystrophy. The fluid is absorbed rapidly, and there have been no infections.

SANFORD, Chicago.

THE EFFECT OF INFECTIOUS FEVER ON BASAL METABOLISM. OTTO BECK, Monatschr. f. Kinderh. **49**:361 (March) 1931.

Elevation of temperature is the most outspoken expression of a number of changes that occur during fever. These changes revolve around the protein metabolism and the acid base relations. Birk was one of the first to notice that fever was accompanied by changes in metabolism. The author carried these studies farther and studied the metabolism as related to the fever of smallpox vaccination in five children. A disease induced artificially lends itself to more accurate study.

The results of observation of four infants show that the basal metabolism does not run parallel to the temperature. There is a prefebrile rise, another and greater rise during the fever, proportionate to the degree of temperature, and later a postfebrile rise. In one child with a chronic osteomyelitis complicated by a spreading cellulitis, the basal metabolism reached its greatest elevation not at the onset of the fever but during the middle of the course, when it was increased to plus 80, and it continued above normal after the fever subsided.

The author concludes from this evidence that increased metabolism, just like fever, is one of the concomitant symptoms of infection and is dependent on changes in protein metabolism rather than on fever.

GERSTLEY, Chicago.

THE NURSING MECHANISM OF INFANTS. ALBRECHT PEIPER, Monatschr. f. Kinderh. **50**:20 (May) 1931.

When a baby takes food three phenomena are observed: sucking, swallowing and breathing. Whether these can occur simultaneously has been discussed by various pediatricians in the past. The author developed a technic for taking tracings and also used the fluoroscope extensively to solve the problem. He shows curves depicting the relationship of breathing and sucking, of sucking and swallowing and of breathing and swallowing. He concludes that in babies fed on the bottle these three processes follow a regular rhythm. With every breath there occur one or two sucking movements, followed by one and occasionally two swallowing movements. The breathing and the sucking movements are not interrupted by the swallowing, which follows its independent rhythm. The author believes that the centers for breathing, sucking and swallowing are closely related, swallowing, after all, being a lower type of breathing; again, swallowing seems to stimulate sucking. Probably the three centers are of common origin.

GERSTLEY, Chicago.

THE RESPIRATION IN ALIMENTARY INTOXICATION. O. BERGER and S. ROSENBAUM, Monatschr. f. Kinderh. **50**: 217 (July) 1931.

It was Czerny's idea that the symptoms of alimentary intoxication are due largely to an acidosis. There is no question of the existence of an acidosis both in clinical cases and in animal experimentation. As proof of his theory Czerny cites the increased respiration. However, the authors point out that respiration is not dependent on one center, but on a number of different respiratory centers which may be influenced by factors other than blood reactions; for instance, various types of breathing in tuberculous meningitis are independent of the chemical composition of the blood.

As regards alimentary intoxication, Bessau and Rosenbaum have frequently emphasized that the characteristic respiration is much deeper than normal and often slower, and Bessau has further noticed the change of respiration from the usual diaphragmatic to a more or less thoracic type. The latter type of breathing is pathognomonic of alimentary intoxication. Inasmuch as this type of breathing can be produced experimentally by the combination of dehydration and endotoxin injection, the authors attempted to solve the problem of acidosis in intoxication by analyzing the expired air of toxic dogs. Their experiments included observations, first, on the normal animal and then on the effect of dehydration alone, the effect of endotoxin plus dehydration and, finally, the effect of endotoxin injection alone.

They found that dehydration alone diminishes the volume of air breathed per minute and per kilogram. The carbon dioxide excretion is diminished while the oxygen intake is increased. The respiratory quotient is sharply reduced, and the results speak against a decided acidosis. In endotoxin poisoning of the dehydrated dog the respiratory volume is increased, and the carbon dioxide excretion and oxygen intake are definitely increased. The respiratory quotient varies considerably, but the findings are in keeping with an acidosis. These determinations were possible only during the stage of increased respiration, and were not made during the period of the slower deeper breathing.

In endotoxin poisoning of the normal animal (only two experiments), there was increased respiratory volume and diminished oxygen absorption.

The authors conclude that though an acidosis may be present in certain stages of alimentary intoxication, this alone does not explain the change of respiration from the diaphragmatic to the thoracic type, nor does it explain the difference in the gas analyses of poisoned dehydrated dogs from those poisoned but not dehydrated.

GERSTLEY, Chicago.

NITROGEN METABOLISM IN THE HEALTHY INFANT. E. ROMINGER and H. MEYER, Ztschr. f. Kinderh. **50**:509 (Feb.) 1931.

In researches in metabolism uninterrupted for a long time Rominger and Meyer have shown that the healthy bottle-fed baby in comparison with the breast-fed baby retains during the entire period considerably more nitrogen, an amount far above the need for growth. It was never shown that there was a period of washing out of nitrogen, not even in an experiment lasting fifty-four days. The nitrogen retention in growing organisms is dependent on the nitrogen offering; the chemical composition of the healthy baby on the bottle must therefore be richer in nitrogen. Babies have a greater capacity for sparing nitrogen than adults. If the nitrogen is diminished in the food, after an amount that has been high, the nitrogen retained in excess is only gradually excreted. But if the nitrogen offering remains high for a long time, the nitrogen retention remains high, the bottle-fed baby retaining more than the breast-fed baby. Further, the nitrogen output, in spite of the greater nitrogen retention, is greater in the bottle-fed baby. This explains why the caloric need of the artificially fed child is increased.

EMERSON, Boston.

THE DIGESTION OF CARBOHYDRATE IN INFANTS: VIII. PHYSIOLOGY OF THE DIGESTION OF MALT EXTRACT. H. PAFFRATH and A. KAESS, Ztschr. f. Kinderh. **50**:553 (Feb.) 1931.

In the absorption of malt extract (Löflund) the easily absorbed carbohydrate disappears with extraordinary rapidity, leaving a small residue which is absorbed slowly or not at all. Extract, fresh or old, is well absorbed. The nonabsorbable residue is composed of pentosans, which occur to the amount of 1.72 per cent, colloidal color substances and, in analogy to the behavior of caramelized cane sugar, uncolored and noncolloidal products of condensation of unknown chemical constitution, which perhaps have something to do with the stimulation of secretion.

Malt extracts are absorbed really with greater rapidity than milk sugar, and are especially suited to the stimulation of "physiologic fermentation" (i. e., fermentation of the small residue not in the small, but in the large, intestine).

EMERSON, Boston.

ALIMENTARY FEVER: VI. IS THERE A "PURE" THIRST-FEVER? H. FINKELSTEIN, Ztschr. f. Kinderh. **50**: 630 (Feb.) 1931.

There is no "pure" thirst-fever, not even in complete water deprivation. In this sense the older observations cannot withstand criticism. Fever occurs if the organism is led from a simple condition of thirst to the stage of beginning dehydration by factors attracting water (diarrhea, vomiting, polyuria), and the presence of water-attracting substances in the food.

EMERSON, Boston.

ALIMENTARY FEVER: VII. PERSPIRATION DURING PNEUMONIC CRISES IN COMPARISON WITH PERSPIRATION DURING THE FALL OF PROTEIN FEVER. L. ROSENWALD, Ztschr. f. Kinderh. **50**: 633 (Feb.) 1931.

Of four cases of pneumonic crises, there was in three a marked diminution, and in one a moderate increase, of extrarenal excretion. Of four cases of defervescing pneumonia, there was in three an increase and in one a diminution. The first series shows that loss of water is not produced by physical processes, but by the lowering of the production of heat internally; in slow defervescence an increase of perspiration is not obligatory; when it occurs, it is in the form of marked sweating, which in itself does not lower temperature. The behavior of perspiration at the close of infectious fevers is accordingly the same as in sodium chloride and protein fever.

EMERSON, Boston.

ALIMENTARY FEVER: VIII. HYPERTHERMIA OR FEVER? H. FINKELSTEIN, Ztschr. f. Kinderh. **50**:637 (Feb.) 1931.

If one considers, on the basis of published observations, how the lack of water, which is common to all kinds of alimentary fever, leads to an increase of temperature, one is forced to refuse the theory of stasis, in the simple form in which it was formulated by Heim and John. The assumptions from which this theory proceeds have not proved themselves to be correct, perspiration, especially, acting directly against expectation; it remains low as long as the temperature is normal; if the temperature increases, it increases also, which means that the height of the body temperature is not dependent on the degree of perspiration, but just the reverse; the degree of perspiration is dependent on the amount of heat formed.

The hyperthermia theory of Rietschel which asserts that, with the lack of water, increased heat may arise from internal work, the overcoming of which is not made possible by the increased evaporation of water, must meet a series of objections hard to answer. The internal work cannot be so great as is assumed by the theory; concentrations and substances produce fever, but do not stimulate an increased formation of heat, and finally, there is a similar contradiction here as with Heim and John, in the behavior of perspiration; under the same conditions perspiration will be increased only if fever occurs; if it does not, perspiration remains the same or may be diminished. It would be expected that just the reverse would occur, since lack of fever, in spite of the increased formation of heat, could be brought about only by straining of the devices for cooling.

Thus the lack of water must stand directly in relation to fever, or, to be precise, not the lack of water but the dehydration. But fever occurs only if the body is forced to give off water from its substance, while simple diminution of fluid. even to the highest degree, runs without fever. Protein, sodium chloride and the other substances causing fever do so only by the fact that the hydrophilia enables them to draw so much water from the physiologic provision that dehydration of the

tissues occurs. There is evidence that not merely the dehydration, but the dehydration in the portal territory, especially in the liver, is significant, and fever occurs only if, because of paralysis of the regulating mechanism, the maintenance of water storage here at the cost of less important territories is insufficient.

What the fever does, on the basis of dehydration, in the end is unknown. The much discussed pyrogenous product of the breaking down of food protein must be discarded, because the presence of food protein affords nowhere an unconditional assumption of an increase of temperature. Bacterial poison can only come in question indirectly as a substance stimulating peristalsis, by which the water output in the intestine is favored. On the other hand, dehydration as such could give off the pyrogenous stimulation. Apparently the assumption is valid that colloidal chemical changes are caused by dehydration, from which the poisons causing fever arise, just as in the destruction of cells and the coagulation of the blood.

The examination of the conditions of origin of fever calls up the question whether the name "alimentary fever" had not better be dropped. "Thirst-fever" no longer seems worthy of recommendation. Only the name "exsiccation fever" meets the situation, and it has the advantage that it expresses the binding of this phenomenon to the complex of exsiccoses.

EMERSON, Boston.

EFFECT OF INSULIN UPON THE BODY WEIGHT OF IMMATURE AND PREMATURE INFANTS. Y. KATSU, Jap. J. Obst. & Gynec. **13**:567 (Oct.) 1930.

The author used insulin in thirty-eight premature infants. The results indicated that the physiologic decrease in body weight could be inhibited. The power of sucking is increased, which stimulates the production of breast milk. The use of small quantities of insulin stimulates metabolism, stabilizes the temperature, reduces the period of icterus and favors the separation of the umbilical stump.

The effect is more marked when a solution of grape sugar is given simultaneously. This solution tends to prevent the secondary reaction from insulin, which is especially liable to occur in these underdeveloped infants. These patients should be hospitalized for treatment.

The prognosis is favorable, and the progress of the infants is good after the use of insulin is discontinued.

ADAIR, Chicago.

MILK SUBSTRATE IN THE PATHOGENESIS OF ALIMENTARY DISTURBANCES OF CHILDHOOD. C. SAITZ, Časop. lék. česk. **68**:300 (March 1) 1929; 339 (March 8) 1929.

A short summary of classifications of alimentary disturbances, as given by Brdlik, Finkelstein, Terrien and Niemann, is presented. Milk factors, as protein, fat, carbohydrate, whey and bacterial by-products, are discussed from the standpoint of tolerance; exudative diathesis, fermentation, putrefaction, idiosyncrasy, metabolism and the production of immunity in infancy and childhood are reviewed. The question of alimentary anemia, iron insufficiency, high milk diets, anorexia, gradual limitation of milk preponderance early in life and the possibility of lighting up tuberculous foci on an insufficient lactovegetable diet are discussed. From 500 to 700 cc. of milk a day is recommended in the various citations for children over 1 year of age. The control of school milk programs should be in the hands of pediatricians.

STULIK, Chicago.

SUMMER HEAT AS ETIOLOGIC FACTOR IN CHILDREN'S DIARRHEA. R. O. LUNTZ, Ohmat det i ozdop. **34**:37, 1930.

It has been known that an internal high temperature in adults influences digestive functions. It usually decreases the appetite for fatty foods and increases thirst and sweat. The reason for high fever in babies is unknown as yet. The

factors to be considered are overheated living quarters and heavy clothing. The experiment shows that there is a decrease in the acidity of the gastric juice. This delays digestion and raises the infection from the large intestine to the small intestine. Of course, there is a loss of water through the skin and lungs, and this leads to dryness of the organs. The effects of heat on the child are: 1. It weakens the digestive function. 2. It changes the intestinal flora, which leads to intestinal infection, producing diarrhea. Sunlight is necessary for the growth of a child, but it must be properly used. Babies up to 1 year of age must take air baths instead of sun baths.

KRUPINSKI, Chicago.

FEEDING BABIES WITH WHOLE LACTIC ACID MILK. N. HINIAKOV, Ohmat det i ozdop. **34**:106, 1930.

At Krakow Institute for the protection of motherhood and childhood the author experimented with whole lactic acid milk to which 10 per cent sugar was added. He found that the babies given this formula gained in weight much more rapidly than those on any other feeding (even human milk), except the breast-fed babies.

KRUPINSKI, Chicago.

THE LEUKOCYTE COUNT DURING ANTIRACHITIC TREATMENT. C. GYLLENSWÄRD and I. JUNDELL, Acta pædiat. **10**:401 (March 15) 1931.

The administration of cod liver oil or irradiated ergosterol in prophylactic doses fails to modify the white blood picture in rickets.

McINTOSH, New York.

TRANSITORY HYPERGLYCEMIA IN INANITION. Y. ÅKERRÉN, Acta pædiat. **10**: 421 (March 15) 1931.

Two cases of transitory hyperglycemia are reported, one in a girl 5 years of age and the other in a boy 11 days of age. The author ascribes the phenomenon mainly to dehydration, supplemented in one case by the presence of fever, and in the other by an altered response to carbohydrate feeding following starvation.

McINTOSH, New York.

Diseases of the New-Born

THE GRASPING REFLEX IN THE NEW-BORN MONKEY. CURT P. RICHTER, Arch. Neurol. & Psychiat. **26**:784 (Oct.) 1931.

The author compared the grasping reflex of the new-born monkey with that of the new-born human infant. The longest period recorded for human infants hanging by both hands was two minutes and thirty-five seconds, while one of the monkeys hung for over thirty-three minutes with one hand. The reflex reaches its maximum after from fifteen to thirty-eight days. It fluctuates from day to day. The reflex reappears under pathologic conditions produced by experimental lesions of the brain and the administration of drugs.

BEVERLY, Chicago.

NUTRITION IN THE NEW-BORN. A. HOTZ, Schweiz. med. Wchnschr. **60**:1201 (Dec. 20) 1930.

In a series of 2,640 newly born children observed during a period of three and one-half years beginning in 1926, 98.5 per cent were partially or entirely breast-fed, and 84.2 per cent were entirely breast-fed. This showed an increase from 72.7 per cent in the year 1925. The artificially fed babies did well. During the first week of life they were given a mixture consisting of one-third milk and two-thirds water.

Carbohydrate to the value of 10 per cent of the milk was added to the formula. The carbohydrate most used was a malt compound the composition of which was not given. During the second week of artificial feeding a mixture of one-half milk and one-half water was used. From this time on, a mixture of two-thirds milk and one-third water was used until whole milk could be used. In all of the formulas 10 per cent carbohydrate was added. The average daily gain in weight was from 13 to 16 Gm.

KREITZ, Ann Arbor, Mich.

CONGENITAL MEGACOLON WITH DISPLACEMENT OF THE CECUM IN AN INFANT THIRTY-FIVE DAYS OF AGE. G. GASTORINA and F. TALIA, Pediatria **39**: 824 (Aug. 1) 1931.

The authors report a case of congenital megacolon with displacement of the cecum in an infant 35 days old. They believe that the anomaly can be explained only as due to arrested development during embryonal life.

SIGNORELLI, New Orleans.

INVESTIGATIONS AND OBSERVATIONS OF BRAIN WOUNDS IN NEW-BORN ANIMALS. F. VIZIOLI, Riv. di neurol. **3**:605 (Dec.) 1930.

Vizioli has investigated the reaction of brain tissue in new-born animals with the intention of studying in particular the phagocytic function of the microglial elements. His interest is particularly concentrated on the possible transformation of the adventitial elements of the blood vessels, of the endothelium and of the blood elements into compound granular corpuscles. From studies reported in the literature it seems established that in adult animals the compound granular corpuscles are derived, in the great majority, from the elements of the microglia. Adventitial elements participate to a lesser degree in the process; the blood elements rarely transform into compound granular corpuscles.

Because the first microglial elements appear in the last periods of embryonal life and multiply rapidly in the first days of extra-uterine life, and because the gray matter shows few microglial elements at birth, Vizioli has investigated the reaction of the brain tissue in new-born animals. His conclusions are that there is a definite difference between the reaction of the tissue of the adult and that of the new-born animal, the difference being more marked in the gray matter where the mass formation of compound granular corpuscles originating from microglial elements is lacking. In the new-born animal, from eighteen to twenty hours after a brain injury, large globoid elements appear which seem to be of hematic origin, probably large lymphocytes, and these elements constitute the majority of the phagocytic elements in the new-born tissue. According to Vizioli, some of these globoid hematic elements undergo a morphologic transformation that recalls the morphology of microglia cells. He therefore advances the hypothesis that microglial elements can originate from blood elements.

FERRARO, New York. [ARCH. NEUROL. & PSYCHIAT.]

CLINICAL HEMATOLOGY IN INFANCY: X. PRIMARY ANEMIA OF THE NEWLY BORN. E. STRANSKY, Ztschr. f. Kinderh. **51**:239, 1931.

On the basis of the small number of cases reported in the literature and two of his own, Stransky pictures the symptomatology, etiology, differential diagnosis, prognosis and treatment of primary anemia in newly born infants. There are two types: The first and more frequent form is characterized by a "nonregenerative blood picture," with no true shift to the left and no embryonal forms, these signs pointing to an insufficient function of the marrow, which may be caused constitutionally. Many patients recover spontaneously, but in the majority one or more transfusions must be done. The differential diagnosis between primary and secondary anemia caused by sepsis, syphilis, hemorrhage and icterus is dis-

cussed. The second type, which is much more rare, shows an embryonal blood picture and hematopoietic foci in the liver, spleen and lymph glands; it has an unfavorable prognosis and reveals many features in common with congenital erythroblastosis, which is quickly fatal. It may be similar to the disease characterized by a profound disturbance of the hematopoietic function. Its etiology is not completely known, and a final judgment is impossible because of the small number of cases. With the cases described here, the number in Germany has gone up to five, to which are to be added ten in America, one each in Holland and Sweden and two in Italy.

EMERSON, Boston.

Acute Infections

USE OF ICTERUS INDEX AND BROMSULPHALEIN TEST IN EXPERIMENTAL YELLOW FEVER. J. A. KERR, Am. J. Trop. Med. **11**:130 (March) 1931.

The author determined the icterus index and bromsulphalein reaction on normal *Macacus rhesus* and on *Macacus rhesus* suffering from yellow fever and other illnesses. In the bromsulphalein test it was found necessary to give intramuscular injections of 5 mg. instead of intravenous injections of 2 mg. The author found the icterus index and bromsulphalein retention test of value in the diagnosis and prognosis of experimental yellow fever in *Macacus rhesus*. An icterus index of 10 or more units on the second day of fever or of 15 or more on the third and fourth day indicated a fatal outcome. With values less than these the outcome was better, the mortality varying from 12 to 23 per cent. A retention of 10 per cent or more of bromsulphalien on the second day of fever or of 15 cent or more on the third day indicated a fatal outcome. With a retention less than this, the outcome was better. The author found the icterus index more reliable and simpler than the bromsulphalein test.

DURPEE, Augusta, Ga.

THE DETERMINATION OF QUININE IN THE BLOOD AS A GUIDE IN THE TREATMENT OF MALARIA. EDWARD V. VEDDER and JOHN M. MASON, Am. J. Trop. Med. **11**:217 (May) 1931.

The authors devised simple methods for determining the amount of quinine in the blood of patients taking it, so as to determine the cause of malarial relapses, if possible. They found that the concentration of quinine in the blood was greatest about one hour after administration by mouth. A single dose of 10 grains (0.65 Gm.) never produced the maximum obtainable concentration in the blood. A great deal of quinine is destroyed in the body, and practically all of it is eliminated by the kidneys after twenty-four hours. The authors thought that this was probably the reason why on a standard treatment one patient was cured and another had relapses. They concluded that the patients who had relapses had never had a sufficient concentration of quinine in their blood, and that it was possible that from 8 to 10 mg. per liter of blood was necessary to kill the parasites, though smaller concentrations injured them. The authors also concluded that further work was necessary to determine the exact concentration of quinine in the blood necessary to be efficacious and still not toxic, and that this method afforded the most intelligent basis for malarial prophylaxis.

BURPEE, Augusta, Ga.

SKIN TESTS AND IMMUNIZATION AGAINST SCARLET FEVER AND DIPHTHERIA. PAUL S. RHOADS, J. A. M. A. **97**:153 (July 18) 1931.

The results of immunization among a large group of student nurses at the Cook County Hospital are recorded. The Dick test proved a reliable indicator of immunity to scarlet fever. Immunization with five doses of scarlet fever toxin

in skin test doses of 500, 2,000, 8,000, 25,000 and 80,000, respectively, proved successful. Immunized nurses did not develop the disease while among 449 unimmunized nurses 14 developed scarlet fever. One nurse who received only the first three doses came down with the disease. The loss of time among those immunized was 0.239 day per nurse.

Five doses of toxin-antitoxin of tested potency or toxoid, followed by retests and more doses when indicated, resulted in better immunization than when only three doses were used. Three cases of diphtheria occurred among 141 nurses so immunized with toxin-antitoxin, and 1 case developed in 424 nurses given a full series of doses of toxoid (2.5 cc. or more). Eighteen cases occurred in 550 nurses unimmunized or insufficiently immunized. Two cases developed in 165 nurses with negative original Schick tests. Complete series of diphtheria toxoid (2.5 cc. or more) immunized 81.4 per cent of the nurses to the point of negative Schick tests, while five doses of toxin-antitoxin of tested toxicity (4.5 cc.) rendered 64.4 per cent immune. The average loss of time because of reactions to toxoid was 0.133 day per nurse.

BONAR, Salt Lake City.

DETOXIFYING AND DISINFECTING PROPERTIES OF SODIUM SALICYLATE: ITS ACTION ON DIPHTHERIA AND TETANUS TOXINS AND ON STREPTOCOCCAL "TOXIC" FILTRATES. KONRAD E. BIRKHAUG, J. Infect. Dis. **48**:212 (Feb.) 1931.

This author concludes that saturated solutions of sodium salicylate have the power of neutralizing diphtheria and tetanus toxins in vitro without destroying their antitoxigenic capacity. Neutralization proceeds in direct proportion to the concentration of sodium salicylate, the duration of contact and the temperature. When the sodium salicylate is combined with diphtheria toxin and immediately injected, the animal dies, but the period of survival is slightly prolonged. An interesting observation is the fact that the salicylate did not act on the so-called toxic filtrates of streptococci, and the author infers that for this reason they may not be true bacterial exotoxins.

TOOMEY, Cleveland.

EXPERIMENTAL PRODUCTION OF SCARLET FEVER BY MEANS OF A SCARLATINAL HEMOLYTIC STREPTOCOCCUS. T. TOYODA, Y. FUTAGI and M. OKAMOTO J. Infect. Dis. **48**:350 (April) 1931.

The Dicks were able to produce scarlet fever experimentally in the human being by the application of *Streptococcus scarlatinae* to the throats of susceptible persons. These authors repeated and confirmed the results of the Dicks. They note that strains newly isolated are more apt to reproduce the disease than old repeatedly subplanted cultures, though both organisms may produce toxin of equal strength.

TOOMEY, Cleveland.

CORRELATION OF OCCUPATION WITH SEROLOGIC REACTIONS FOR BRUCELLA ABORTUS. AXEL THOMSEN, J. Infect. Dis. **48**:484 (May) 1931.

This worker tested serologically the blood of 272 persons whose occupation caused them to come in contact with cattle. The blood was tested for agglutinins and complement-fixation bodies for *Bacillus abortus*. The author concludes that most of these become infected through the treatment and care of animals infected with *Bacillus abortus*, since he found these serologic factors present in such a high percentage of these contacts. He adds, however, that caution must be emphasized in serologic interpretations, since the serums of healthy persons employed in testing laboratories are sometimes positive. He concludes that milk has no proved connection with the reactions.

TOOMEY, Cleveland.

SPORADIC CELLULITIS AND ABSCESS DUE TO STREPTOCOCCUS EPIDEMICUS. I. PILOT and D. J. DAVIS, J. Infect. Dis. **48**:505 (May) 1931.

The authors recount the various clinical conditions that may be caused by *Streptococcus epidemicus,* among which are cellulitis, subcutaneous abscesses, suppurative lymphadenitis, peritonsillar abscesses, otitis media, mastoiditis, meningitis and empyema.

TOOMEY, Cleveland.

DISSOCIATION OF HEMOLYTIC STREPTOCOCCI FROM ERYSIPELAS, SCARLET FEVER AND SEPTIC SORE THROAT. RUTH TUNNICLIFF, J. Infect. Dis. **48**:511 (June) 1931.

The author notes the ordinary results after culturing various streptococci from persons with scarlet fever, erysipelas and septic sore throat. Her object was to study the variants from the normal after such procedures as frequent transplanting after injection into mice, etc. She concludes that many strains of hemolytic streptococci from patients with these three clinical conditions remain stable for years. A few strains may dissociate, but most of the latter revert to the original streptococcus under proper conditions. This factor of dissociation may account for some of the difficulty in differentiating erysipelas from scarlet fever streptococci.

TOOMEY, Cleveland.

COMPLEMENT-FIXATION AND AGGLUTINATION TESTS IN BRUCELLA ABORTUS INFECTION. K. T. SASANO, D. CALDWELL and E. M. MEDLAR, J. Infect. Dis. **48**:576 (June) 1931.

The serums from 1,000 persons were examined, and because 96 revealed a positive complement fixation and 78 a positive agglutination while only 5 were from patients who had undulant fever, the authors concluded that a positive diagnosis should be made only when a positive blood culture exists or when the titer of the agglutinability of the blood serum is well above 1:45.

TOOMEY, Cleveland.

EXPERIMENTAL POLIOMYELITIS. P. H. HARMON, H. J. SHAUGHNESSY and F. B. GORDON, J. Prev. Med. **5**:115 and 139, 1931.

Prior to the onset of experimental poliomyelitis in *rhesus* monkeys following intracerebral inoculation of virus, changes occur in the body temperature, in the numbers of polymorphonuclear neutrophilic leukocytes in the blood and in the cell and globulin contents of the cerebrospinal fluid. These changes are analogous to those that occur in poliomyelitis in man. The first constant alteration detectable in the preparalytic stage of the experimental disease is the change in the body temperature. In many, but not all, monkeys the preparalytic increase in the numbers of neutrophilic leukocytes is coincident with the rise in the body temperature; in a few cases the change in the leukocyte count occurs a day or two after the rise in the temperature. Changes in the spinal fluid occur definitely one or two days after the changes in the temperature, except in a few animals in which the two changes are observed simultaneously. Alterations in the velocity of the sedimentation of the erythrocytes occurred only after the onset of paralysis, usually after the monkey was prostrate from an extension of the disease.

Our criterion for abortive poliomyelitis in monkeys is absence of paralysis, but presence of symptoms and of changes in the spinal fluid or of symptoms and of an increase in the body temperature and in the numbers of neutrophilic leukocytes, the symptoms, the changes in the spinal fluid and the increase in the temperature and in the numbers of leukocytes occurring after a period of incubation and resembling those observed in the preparalytic stage of the ordinary form of the disease. Following 555 intracerebral inoculations in 350 monkeys, only 10 cases of abortive poliomyelitis occurred. We found 7 instances of "missed infection," in which a

certain dilution of a virus caused no paralysis in a monkey, although a monkey receiving a higher dilution became paralyzed. Some of these may have been cases of abortive poliomyelitis, although they did not conform to our criterion. Two cases in which paralysis occurred thirty-three and fifty-one days, respectively, after inoculation were probably cases of relapsing poliomyelitis. Abortive and relapsing poliomyelitis and "missed infections" seem to be the result of differences in susceptibility in individual monkeys, rather than of mild infection with an attenuated virus.

AUTHORS' SUMMARY.

EXTREME LEUCOCYTOSIS IN PERTUSSIS. ARTHUR F. ABT, M. Clin. North America **14**:1229 (March) 1931.

Most of the reported instances of hyperleukocytosis in pertussis have occurred in cases complicated by pneumonia. In the case reported by Abt there was no indication of pneumonia or other complications except a short series of convulsions which occurred during the first three days of observation. The progress thereafter was that of a typical case of pertussis. The uncommon features of this case were an extreme leukocytosis of 213,330 with a preponderance of lymphocytes (from 60 to 70 per cent). The leukocytosis gradually declined to 88,000 on the fifth day of observation, to 58,000 on the tenth and to 21,000 on the fifteenth. On the later date, the differential count showed polymorphonuclears 19, small lymphocytes 66 and large lymphocytes 13. The child made an uneventful recovery. Hyperleukocytosis with a white cell count of from 100,000 to 200,000 or over, except in extremely rare and isolated instances, occurs only in leukemia or pertussis.

SMITH, Ogden, Utah.

ACUTE INFECTION IN CHILDHOOD (MEASLES). GEORGE B. BADER, M. Clin. North America **14**:1475 (May) 1931.

The injection of whole blood from selected donors represents the easiest, least objectionable and most practical means of preventing measles, particularly at the onset of an epidemic. Discrimination in the selection of donors is advised. If choice is possible, older children of the family who have had measles, adults who have had the disease not more than from ten to fifteen years previously, and interns and nurses who have had measles and who are in frequent contact with the disease should be selected. The author is not prepared to state that attenuated disease following the injection of whole blood confers permanent immunity. Thirty cubic centimeters of whole blood, 15 cc. in each buttock, is suggested as an arbitrary dose, but much less blood from a good donor may be sufficient.

SMITH, Ogden, Utah.

IMPORTANT ASPECTS OF MEASLES. PHILIP M. STIMSON, New York State J. Med. **31**:352 (March 15) 1931.

The importance of fever as the first symptom of measles is pointed out. The measles line, red macule and Koplik spots are described. The author stresses the importance of isolation in the treatment for measles.

AIKMAN, Rochester, N. Y.

REPORT OF COMMITTEE TO FORM A PLAN TO MAKE TOXIN-ANTITOXIN AVAILABLE TO EVERY CHILD IN THE STATE (REPORT TO HOUSE OF DELEGATES, MEDICAL SOCIETY OF THE STATE OF NEW YORK). New York State J. Med. **31**:564 (May 1) 1931.

A five year program was started in 1926. While great headway has been made, the committee finds a "lack of enthusiastic cooperation on the part of the medical profession." In certain sections the practitioners helped to secure nearly 100 per

cent results. In other counties they seem willing to leave the problem to the health department. Physicians should awaken to the realization that they "must assume the leadership in community health problems." The charts show that from 1926 to 1930, 726,550 received free injections of toxin-antitoxin.

AIKMAN, Rochester, N. Y.

IS THE HAEMOLYTIC STREPTOCOCCUS ACCEPTABLE EPIDEMIOLOGICALLY AS THE AETIOLOGICAL AGENT OF SCARLET FEVER? T. TOYODA, C. KUROI, J. MORIWAKI and Y. FUTAGI, Brit. J. Child. Dis. **28**:89 (April-June) 1931.

On examination of 1,545 persons in Dairen, Manchuria, the authors found that in 748 primary school children and others a toxigenic streptococcus could be detected in the throat in 14.4 per cent. There were 14.7 per cent of such positive cases among 575 with a positive Dick reaction, 24.5 per cent among 61 with a negative Dick reaction, 27 per cent among 89 nurses attending patients with scarlet fever and 28 per cent among 72 members of families of patients with scarlet fever.

In testing ten strains of what was considered as the typical β type of the hemolytic streptococcus isolated from healthy throats, it was found that 60 per cent produced Dick toxin, but only two strains had the capacity to produce as powerful a toxin as the scarlet fever streptococcus.

Of 417 patients with scarlet fever, 233 (56 per cent) had throat cultures that were negative for hemolytic streptococci before leaving the hospital (mostly in the fifth week). No case of scarlet fever developed in these families, whereas in the families of those leaving the hospital with positive throat cultures 7 cases of scarlet fever developed within a week after their return.

From 1921 to 1927, 2,264 cases of scarlet fever and 942 cases of erysipelas were observed in the twenty-two hospitals of the South Manchuria Railway Company. Among the 1,264 cases of scarlet fever there were 197 Chinese, while among 942 cases of erysipelas there were 341 Chinese, showing the high incidence of erysipelas in contrast to scarlet fever. Among the Chinese there are a large number giving negative Dick reactions. The females are more susceptible to scarlet fever while the males are more prone to erysipelas. Scarlet fever is more prevalent among children from 3 to 6 years old, while erysipelas is more common in babies under 1 year and in adults. Scarlet fever and erysipelas treated in the same hospital in the same period show a parallel course as regards the rise and fall in their incidence. Scarlet fever is more prevalent and more severe in the cold and temperate zones, and more cases occur during the cool months.

Scarlatinal streptococci can stand cold remarkably better than heat; dry weather better than wet, and darkness better than daylight. In Africa, India and North America the colored people show a far lower morbidity rate than the whites.

While nonscarlet fever streptococci (pyogenic streptococci, etc.) can also produce Dick toxin, scarlet fever streptococci are found to have the strongest power to produce the toxin. Erysipelas streptococci are the nearest approach to scarlet fever streptococci as far as the production of Dick toxin is concerned.

LANGMANN, New York.

EARLY NEPHRITIS IN SCARLATINA. E. ASHWORTH UNDERWOOD, Brit. J. Child. Dis. **28**:114 (April-June) 1931.

In a girl, aged 16 years, acute nephritis was discovered on her admission to the hospital on the second day of her disease. Evidence of nephritis, chiefly albumin and red blood corpuscles, persisted for several months. An attack of tonsillitis four and a half months after the onset of scarlet fever produced an exacerbation of the nephritis. However, the tonsils and adenoids were removed soon after this attack and the patient was discharged about six weeks later, the urine having been apparently normal for a fortnight. A report four years later stated that the

patient was suffering from chronic nephritis. The author is inclined to the view that an organism other than *Streptococcus scarlatinae* caused the initial nephritis.

LANGMANN, New York.

SOME PAEDIATRIC EPONYMS: III. KOPLIK'S SPOTS. W. R. BETT, Brit. J. Child. Dis. **28**:127 (April-June) 1931.

The author quotes largely from Koplik's three papers which called attention to the diagnostic sign now associated with his name. The first, entitled "The Diagnosis of the Invasion of Measles from a Study of the Exanthem as It Appears on the Buccal Mucous Membrane," was published in 1896. A short biography of Koplik follows.

LANGMANN, New York.

THE CONCENTRATION OF THE PROTECTIVE SUBSTANCE IN ANTIPOLIOMYELITIS SERUM. W. T. J. MORGAN and R. W. FAIRBROTHER, Brit. J. Exper. Path. **11**:512, 1930.

From the experimental results obtained with the serum from a horse immunized with living poliomyelitic virus, it would appear that the protein precipitated at a relatively low concentration of ammonium sulphate is uniformly much more potent in antiviral action per unit weight of protein than that precipitated at higher concentrations of this salt; and, in conformity with this result, the protein thrown out of solution by dialysis of the immune serum and the serum protein that is insoluble in saturated solution of sodium chloride have been shown to possess potent antiviral properties. The evidence indicates that in this serum there is a general distribution of the antibody throughout the serum proteins, since carefully fractionated preparations of the pseudoglobulin and albumin possess definite, although slight, virus-neutralizing properties.

AUTHORS' SUMMARY.

FURTHER INVESTIGATION ON THE VARIOLA-VACCINIA FLOCCULATION REACTION. J. CRAIGIE and W. J. TULLOCH, M. Research Council, special report series, no. 156, 1931.

Investigations of material from cases of variola, major and minor, and vaccinia in man and animals corroborate the "variola-vaccinia flocculation reaction" as specific and of considerable diagnostic value. Immune flocculating serum of high titer definitely confers passive immunity, and in some instances the activity of such serums in this respect is so great that 1 cc. of serum per kilogram of body weight may protect against a very large multiple of the minimum infecting dose administered intradermally, by scarification or even by the intratesticular route.

SANFORD, Chicago.

SERUM PROPHYLAXIS IN MEASLES. CHARLES ANDERSON and F. GÉRARD, Arch. Inst. Pasteur de Tunis **19**:435, 1930.

Following the principles implied in the idea of local immunization, persons who had come in contact with patients with measles but who had not previously had the disease were treated three times daily by a drop of convalescent serum in each eye. Although only thirty patients are reported on thus far, all of those treated in this way escaped the disease, whereas measles developed in other contacts within the usual period.

M. S. MARSHALL.

THE ACTION OF THE GLUCOSIDES OF SQUILL IN THE NEPHRITIS OF SCARLET FEVER. A. STROE and P. KLINGER, Paris méd. **1**:357 (April 11) 1931.

The authors used glucosides of squill in twenty-one cases of postscarlatinal nephritis with success. It is given intravenously, 1 cc. per day.

SANFORD, Chicago.

PROPHYLAXIS AGAINST DIPHTHERIA BY LÖWENSTEIN'S PROTECTIVE SALVE. A. ROSENBLÜTH, Ztschr. f. Kinderh. **50**:775 (March) 1931.

Of 290 boys, from 11 to 18 years old, in an institution, 51 per cent gave negative Schick reactions before, and 67.5 per cent after, inunction with Löwenstein's salve. Of 120 boys who gave positive Schick reactions, 36 per cent gave negative reactions fifty days after the first inunction and twenty-two days after the third; in 64 per cent the reaction was unchanged (positive). Of 108 boys, 32.5 per cent showed a negative reaction and 67.5 per cent a positive reaction six months after the first inunction and five months after the last. Prophylaxis by Löwenstein's salve fulfils the conditions of being easy to apply and harmless, but, measured by the outcome of the Schick reaction, has not the dependability desired.

EMERSON, Boston.

Chronic Infections

CONGENITAL BONE SYPHILIS; PRELIMINARY REPORT: ROENTGENOLOGIC STUDY WITH NOTES ON THE HISTOLOGY AND PATHOLOGY OF THE CONDITION. E. P. PENDERGRASS and R. S. BROMER, Am. J. Roentgenol. **22**: 1 (July) 1929.

A discussion of endochondral, intramembranous and general growth and development of bone is followed by a detailed study of the osteochondritis, diaphysitis and periostitis of congenital syphilis, scurvy and rickets. The summary follows: Epiphysis: The outline of resting and proliferative cartilage in rickets and syphilis is swollen, but in scurvy is of normal size. The epiphyseal center in rickets has a motheaten appearance throughout; in scurvy a distinct shadow is present, with the characteristic ground-glass appearance of the center; and in syphilis the periphery is intact; localized areas of rarefaction within the center are often present in close proximity to the periphery.

Diaphyso-Epiphyseal Junction: The zone of temporary calcification and the zone adjacent to it on the shaft side: 1. In rickets this zone gradually disappears; it is always a thin line, and is broken at intervals if not wholly absent. In syphilis it persists as a dense, broad zone. In scurvy it shows as a distinct widened dense zone. 2. In healing rickets a new zone of temporary calcification is formed with an intervening layer of osteoid bone. In syphilis a new zone is formed without the characteristic osteoid layer intervening. In healing scurvy the zone becomes increasingly denser and wider. 3. In rickets thick and coarse trabeculae are found in the shaft, in the adjacent zone. In syphilis this adjacent zone has a more evenly blurred appearance, while in scurvy the framework marrow zone of decreased density can easily be recognized in the cases clinically beyond the latent or subacute stage. 4. Cupping of the diaphyseal ends is present only in rickets. In scurvy the lateral spurs, or early roentgen evidence of hemorrhage, project at right angles to the shaft at the diaphyseal ends. In syphilis neither cupping nor lateral spurs can be found. 5. In rickets the fraying of the cupped area can be traced into the resting cartilage of the epiphysis. In syphilis fine, thin projections can be seen occasionally in the first and second stages of osteochondritis with the aid of a magnifying glass. They also extend into the cartilage, but these have a more even, fine and uniform arrangement. In scurvy the outline of the zone of temporary calcification on the epiphyseal side shows a distinct, sharply outlined margin. Periosteal changes are present in all three diseases. Periostitis rarely occurs alone in congenital syphilis; it usually accompanies advanced osteochondritis, and is more frequent in older infants and children. In excellent roentgenograms perpendicular striations can be noted in syphilis. The periosteal change in rickets is a homogeneous osteoid deposition of bone. In scurvy periosteal thickening is the result of the calcification and disappearance of subperiosteal hemorrhages. The manifestation of the healing stage is usually accompanied by characteristic changes in the epiphyseal centers of ossification. The lack of periosteal proliferation in congenital syphilis along the posterior borders of the femur is another diagnostic sign.

A case of acute leukemia showed essentially normal long bones except for an extremely marked increase in the width of the zones of temporary calcification. Progress of congenital syphilis under treatment is as follows: broadening and rarefaction of the shadow at the diaphyseal extremity, the reappearance and intensification of trabeculae in the area of decreased density, a gradual change to normal and regular bone growth of the irregular densities at the end of the shaft. Periosteal changes were slower in returning to normal. In some cases the changes disappeared without any treatment.

Roentgenograms and a complete bibliography are given.

STULIK, Chicago.

THE TRANSMISSION OF SYPHILIS BY BLOOD TRANSFUSION. SILIK H. POLAYES and MAX LEDERER, Am. J. Syph. **15**:72 (Jan.) 1931.

The author warns against the possibility of transmitting syphilis through blood transfusions. There are two main sources of this danger. One is the unreliability of the Wassermann reaction at certain times, and the other arises from the fact that certain purchasers of blood for transfusions are perhaps negligent in checking the blood of the donors often enough. Instances of transmission through both mediums are cited.

ROYSTER, University, Va.

THE TREATMENT OF PERICARDITIS WITH EFFUSION BY INJECTION OF AIR AND IODIZED POPPY SEED OIL INTO THE PERICARDIAL SAC. W. ACKERMANN, Am. Rev. Tuberc. **24**:98 (Aug.) 1931.

This is a final report, with autopsy findings, on a case of chronic tuberculous pericarditis, in which forty-three treatments of the pericardium were performed, thirty-eight consisting of aspirations, followed immediately by injections of air. Two of the thirty-eight treatments were supplemented by injections of (1) iodized poppy seed oil 40 per cent and (2) gomenol oil in a 4 per cent solution. Tappings and injections of oil, iodized oil and gomenol oil into the pericardial sac actually prolonged the patient's life for a year and a half. Iodized oil proved to have a greater curative value than gomenol oil, as the former established an immediate reaction which was followed by beneficial consequences; the gomenol oil also established a reaction, but it was very faint and had no effect on the patient's condition. The fatal outcome was due to a highly virulent type of tuberculous infection, proved by numerous positive tests.

SMITH, Ogden, Utah.

TUBERCULOSIS, RICKETS AND THE DIET. G. J. HILDEBRAND, Wisconsin M. J. **30**:445 (June) 1931.

The author believes with others that the beneficial action of fats in pulmonary tuberculosis may be because of their coming into direct contact with lung tissue following their absorption by the lymphatics. Some fats, like cod liver oil, tend to retard the growth of the tubercle bacillus. African natives who eat much fat have comparatively little tuberculosis. A change in their diet and habits in civilization makes them very susceptible, as it does the Indian.

The incidence of rickets and tuberculosis shows a striking parallel increase when the food supply becomes poor, especially in fat and food of animal origin. Rachitic animals inoculated with tuberculosis organisms develop tuberculosis much more easily than the nonrachitic. Chicken-breasted persons are especially prone to have tuberculosis. This brings up the possibility of rickets causing a permanent deleterious calcium metabolism, increasing susceptibility to tuberculosis. In emphasizing vitamins and vegetables, one must not forget the importance of fats and proteins.

JANNEY, Milwaukee.

LOCAL AND GENERAL PROBLEMS IN TUBERCULOSIS ADMINISTRATION. HARRY J. RAE, Edinburgh M. J. **38**:152 (March) 1931.

The author discusses the milk supply of Scotland, which, while improved, still contains tubercle bacilli in 5 per cent of the samples. A new law will require tuberculin-tested animals in the herds supplying milk for school children. The institutional treatment for pulmonary tuberculosis, especially in the city of Aberdeen and adjacent counties, uses up the largest part of the budget for the control of this disease. The aftercare takes place in tuberculosis colonies, institutions and local workshops.

There are two preventoria near Aberdeen where pretuberculous children with stigmas of tuberculosis are carefully nursed and treated. Preventoria should be established generally in Scotland because of the preventive work which these institutions are doing.

NEFF, Kansas City, Mo.

THE MANTOUX TEST. WILFRID F. GAISFORD, Lancet **1**:521 (March 7) 1931.

The Mantoux test was performed as a routine on 400 children at the East London Children's Hospital, and during an interval between the routine testings it was applied to 100 selected cases. The main sources or error to which the test is liable are the following: (*a*) suppression of the reaction due to diminution of skin sensitivity during acute illness associated with fever; (*b*) suppression due to the severity or extent of the tuberculous infection, e. g., miliary tuberculosis; (*c*) suppression due to altered allergy as the result of recent illness, e. g., during convalescence after measles.

One-tenth cubic centimeter of 1:1,000 old tuberculin was injected intradermally, and readings were taken twenty-four and forty-eight hours later. The acute reactions in young children and infants proved to be of bad prognostic significance, but in older children this was not always so. Of the 400 unselected cases, 86 (21.5 per cent) showed positive results.

LANGMANN, New York.

CHRONIC PULMONARY INFECTIONS IN CHILDHOOD. ALLAN K. KRAUSE, Tubercle **12**:344 (May) 1931.

Recent observations on the incidence and nature of tuberculous infection in infancy and childhood are dispelling many firmly entrenched misconceptions concerning the pathogenesis and prognosis of the disease as it occurs in early life. That so large a proportion of children known to have been infected manifest no signs of activity subsequently is indicative of a high degree of resistance. The benign course of the infection, as commonly found, justifies the conclusion that "by and large, tuberculosis as such, is essentially a non-progressive infection, in not only the adult, but in the child also; and unless all signs fail, in the infant likewise, if not less. . . . As for the period of childhood, all signs point to a condition of extraordinarily high resistance; childhood is really mankind's 'golden age' as regards tuberculosis." However, this more hopeful attitude toward tuberculosis in early life and the predominance of benign types at this age should not blind the physician to the more serious possibilities of the disease. Infection as such, which does not arouse any physiologic (functional) response, may be viewed with equanimity; not so, however, if such symptoms as undernutrition, irritability, asthenia and lowered vascular and muscular tone accompany infection. These symptoms spell "activity," even in the absence of anatomic signs. Tuberculosis in children should be regarded as active or inactive, with no middle ground of latency to blur the picture. To fail to trace to their source such physiologic disturbances as those mentioned is as grave an error as failure to recognize tuberculous infection in childhood until anatomic signs are present.

The occurrence of chronic nontuberculous types of pulmonary infection has received comparatively scant attention from members of the profession in general.

Even in early life, focal changes of a nontuberculous type are not rare, and frequently not only are a drag to the normal development of the child, but may lay the foundation of lifelong invalidism. The number of persons at tuberculous resorts incapacitated by bronchiectasis indicates that a large group must be on its way to this hopeless condition. For this reason alone it is important to detect any focal changes of an infectious nature occurring in childhood. The beginnings of this chronic infection in childhood may be no less misleading and impenetrable than those assumed by tuberculosis. The most frequent complaint is that of catching cold, perhaps too often attributed to disturbances of the upper respiratory tract, throat, ears, tonsils and sinuses. Then follow winter cough, bouts of fever and later recurring bronchopneumonia. It is certain that quite early in the process, focal infection occurs in the chest, usually on one side and extending into the lower lung fields. The recurring bronchopneumonia localizes in this region again and again, with gradual extension of the focal infection and later possible abscess or bronchiectasis. The outlook in the later stages is hopeless, but it is not too much to believe that with early recognition, progress may be checked at a point short of permanent invalidism.

SMITH, Ogden, Utah.

A FATAL CASE OF TUBERCULOSIS FOLLOWING VACCINATION WITH B C G. E. JASO, Arch. de méd. d. enf. **34**: 169 (March) 1931.

After practicing oral administration of B C G for three years with encouraging results, Jaso decided to employ the subcutaneous method on which he promises to report in extenso. One case of special interest is described in advance. A girl, aged 13 months, was admitted to a foundling asylum in Madrid on Aug. 28, 1929, suffering from undernourishment and advanced rickets. The Mantoux test was made on three occasions, in the strength of 1:1,000, with completely negative results; the first test was performed forty days, the second seventy-five days and the last ninety days, after admission. On the basis of these observations, the infant was vaccinated subcutaneously with B C G on Nov. 30, 1929, the site of the injection being the scapulohumeral region and the dosage 0.0125 mg. No local or general reaction was noted. In the interval separating the second from the third Mantoux test, subcrepitant râles were discovered in the base of both lungs, but the succeeding tuberculin test still being negative, B C G was injected eleven days after râles were noted. During the following six months, in spite of every care the baby showed no improvement in strength or vigor and very little in weight; it was removed to the infirmary. Here it was found that there was afternoon elevation of temperature, and the observations on the chest were suggestive, but a Pirquet test gave negative results as did examination of the stomach contents for tubercle bacilli. Suddenly the Mantoux test became positive; signs of cavitation were clearer, the appetite failed, fever was almost continuous and roentgen examination revealed advanced pulmonary tuberculosis. A few days later the patient died; autopsy confirmed the diagnosis in every respect. A terminal miliary process was present with caseous pneumonia and granular hepatitis.

Several questions naturally arose: Was this infant tuberculous before injection? Was it free from infection before inoculation? Did the B C G vaccination arouse a definite disease process? It is conceivable that an infection may be so benign as not to provoke a tuberculin reaction and that this mild form may be activated by the subcutaneous inoculation of B C G. In any event, the rapidly fatal termination of this case, after exhibition of the specific prophylactic arouses in the author's mind the suspicion that the latter may not be as inoffensive as reports would have one believe.

AMESSE, Denver.

VACCINATION WITH B C G. A. WALLGREN, Nourrisson **19**:53 (Jan.) 1931.

This is a report on the results obtained by intradermal vaccination with B C G in 106 infants, all coming from homes where active tuberculosis existed. Wallgren

is the medical director of the Children's Hospital at Gothenburg, Sweden. His technic is described in *The Journal of the American Medical Association* (**91**:1876 [Dec. 15] 1928).

Of the 106 infants inoculated, 44 were kept free from subsequent exposure to tuberculous infection. Two of these died of acute pneumonia. The others remained well. Of the 63 who were exposed after vaccination, none was exposed until after a positive allergy had developed, as shown by a positive intracutaneous tuberculin reaction.

The time of exposure varied from two months to three years after vaccination. None of these infants has shown evidence of tuberculosis in a form clinically demonstrable. In 2 cases roentgenograms have shown a suggestive involvement of the hilar glands.

All these infants were isolated from tuberculous contacts immediately after birth, and the author emphasizes the fact that this isolation as well as the rôle played by the vaccination must be taken into consideration in evaluating the results. However, he believes that the effect of the vaccination is important.

McCLELLAND, Cleveland.

TUBERCULOUS MENINGITIS IN A TWO YEAR OLD INFANT VACCINATED WITH B C G. G. BLECKMANN and A. E. LEVY, Nourrisson **19**:110 (March) 1931.

An infant received three doses of B C G vaccine at the ages of 3, 5 and 7 days, respectively. It was exposed to tuberculosis from the sixteenth to the nineteenth month by an elder brother who subsequently died of pulmonary tuberculosis. The infant became ill at the age of 26 months with gastro-intestinal symptoms. Convulsions, hemiplegia and involvement of the cranial nerves followed in a few days and then the typical signs of meningeal irritation. A cutaneous tuberculin test made at this time was negative. The examination of the spinal fluid showed normal globulin, 40 cells (60 per cent polymorphonuclears) and the presence of acid-fast bacilli. Death followed in a few days. No autopsy was performed.

McCLELLAND, Cleveland.

DIAGNOSIS OF THE ACTIVITY OF PULMONARY TUBERCULOSIS. E. LEURET and J. CAUSSIMON, Rev. de la tuberc. **12**:293 (March) 1931.

This essay of almost 200 pages is, in reality, a fairly comprehensive monograph on pulmonary tuberculosis. As a preliminary to their main thesis, the authors consider the classification of the various forms of tuberculosis with their pathology. The clinical and roentgen aspects of the disease are thoroughly reviewed, and the various laboratory procedures evaluated. The authors conclude that an idea of the activity of a tuberculous pulmonary lesion cannot be arrived at except by study of the signs—clinical, roentgen and serologic—considered in series and compared with each other. A comparison of the observations at different stages of the disease alone permits an affirmation of the activity of the lesion.

SMITH, Ogden, Utah.

MILD CASES OF OPEN PULMONARY TUBERCULOSIS IN CHILDREN. BURCKHARDT and SATTLER, Schweiz. med. Wchnschr. **61**:351 (April 11) 1931.

The prognosis in open tuberculosis in children at an early age and during puberty is especially poor, according to G. Simon. In at least 33 per cent of the cases the patients die and, at most, 10 per cent clear up, these being pneumothorax cases.

In the author's series of cases in the Children's Sanatorium at Davos approximately 50 per cent of the patients with open tuberculosis were discharged free from symptoms. They report a series of six cases in children from 11 to 16 years of age. These patients were not acutely ill, and the symptoms were those of common grip or, as they called it, "apical catarrh." The roentgenograms

showed changes in the apexes or the upper lobes. The tuberculin tests were positive. These cases cleared up within the course of a few months.

These cases were classified as "the abortive tuberculosis of Bard or of Neumann." The authors suggested that this type be called "anauscultatory tuberculosis" in the sense that there are relatively few specific findings. The term "anauscultatory" does not mean that one does not hear anything that is abnormal, but that the auscultatory findings are not in proportion to roentgen and autopsy findings.

The findings were: (1) a mild diffuse bronchitis, (2) a mild decrease in resonance, (3) rough or harsh breath sounds over the hilus and apexes, (4) no râles, (5) positive roentgen findings and (6) a positive tuberculin test.

Burckhardt and Sattler believe that there exists in children of school age a type of mild open pulmonary tuberculosis. This type they call "anauscultatory open pulmonary tuberculosis." It is characterized by indefinite auscultatory and percussion findings. Examination of the sputum gives positive results. The practical value lies in the good prognosis.

KREITZ, Ann Arbor, Mich.

A MODIFICATION OF THE PERCUTANEOUS REACTION OF MORO. M. SCARZELLA, Riv. di clin. pediat. **29**:473, 1931.

In order to render the Moro tuberculin test more sensitive, the author advises washing the skin at the site of the inunction — preferably the breast or the back — with a 10 per cent solution of sodium hydroxide. This should increase the penetration of the tuberculin.

The modified reaction was tried on 261 infants. The conclusion is that this procedure is more sensitive than the Pirquet, Trambusti and Mantoux tests when a solution of 1 : 10,000 is used. The intradermal test (Mantoux) using a solution of 1 : 1,000 is more sensitive than the modified Moro test.

HIGGINS, Boston.

THE VALUE OF INTRADERMAL TESTS WITH THE SPINAL FLUID OF PATIENTS WITH TUBERCULOUS MENINGITIS. B. TRAMBUSTI, Riv. di clin. pediat. **29**:563, 1931.

The author concludes that material obtained from the cerebrospinal fluid of patients with tuberculous meningitis is unsatisfactory for use in skin tests as a diagnostic procedure.

HIGGINS, Boston.

A CASE OF PSEUDOPARALYSIS OF PARROT WITH LUXATION. M. O'DONNELL and S. COSSOY, Rev. de especialid. **6**:31 (June) 1931.

A case of Parrot's disease is presented, together with roentgenograms.

SANFORD, Chicago.

SOME MANIFESTATIONS OF LEPROSY. A. PENA CHAVARROA and FRANCISCO DE P. BARRERA, Rev. méd. latino-am. **16**:814 (March) 1931.

The trophic manifestations of leprosy are not always symmetrical. Several cases are illustrated with great variation in the atrophy and contractions of the interosseous muscles of the hands. The nervous types may vary considerably in their bilateral and symmetrical distribution.

DWYER, Kansas City, Mo.

RESULTS OBTAINED WITH ACETARSONE IN THE TREATMENT OF CONGENITAL SYPHILIS. A. BRATUSCH-MARRAIN, Arch. f. Kinderh. **92**:26 (Nov. 28) 1930.

The author reviews the results with acetarsone obtained during two years at the Graz Clinic. The dose is from 0.01 to 0.02 Gm. per kilogram and may be given by mouth. It is useful in ambulatory patients as there is no reaction. He believes it to be the best substance for treating patients with congenital syphilis.

SANFORD, Chicago.

FEVER THERAPY IN CONGENITAL SYPHILIS. G. SOEKEN, Arch. f. Kinderh. **92**:216 (Feb. 13) 1931.

The author used fever therapy in thirty-five cases of resistant syphilis. In nine cases the fever agent was blood from patients with recurrent malaria, and in twenty-six cases blood from patients with tertiary malaria. The dose was from 2 to 5 cc. of blood. The height of the action was six days for the recurrent form, and from four to twenty days for the tertiary. The results were as follows: Of six children with syphilis of the central nervous system, four were clinically improved and five showed serologic clearing. Of seven with bad neurologic symptoms and positive Wassermann reactions, four were clinically improved and six had negative Wassermann reactions. One child who had a return of symptoms was unchanged. Of five children with positive Wassermann reactions three became negative, and of twelve Wassermann-fast cases seven showed improvement.

SANFORD, Chicago.

THE OCCURRENCE OF THE LUETIN REACTION IN CONGENITAL SYPHILIS. THERESE KINDLER, Dermat. Wchnschr. **92**:538 (April 11) 1931.

"Luotest," a luetin prepared by Müller and Brandt from the testes of syphilitic rabbits, was used in 103 cases of congenital syphilis. In the first year all tests were negative; between the first and fourth year, 25 per cent were positive; from the fourth to the fourteenth year, 93 per cent; from the fourteenth to the twentieth year, 80 per cent, and beyond the twentieth year, 83.3 per cent were positive. The test is considered a valuable addition to the Wassermann reaction in this type of syphilis.

TAUSSIG, San Francisco.

IS EPIDERMODYSPLASIA VERRUCIFORMIS (LEWANDOWSKY-LUTZ) AN INDIVIDUAL DERMATOSIS? L. N. MASCHKILLEISSON, Dermat. Wchnschr. **92**:569 (April 18) 1931.

The cases previously reported (twenty-one) are listed in tabular form. The author describes a typical instance in a patient 23 years of age in whom the cutaneous condition first appeared when he was 2 years old. The histology is described. A second case is reported in which the eruption was limited to the forehead and in which the histology was similar to that of the typical case of epidermodysplasia. The author concludes: 1. This condition is distinct from the verrucae. 2. It belongs to the group of skin dystrophies connected with the precancerous conditions. 3. The histologic characteristic is "clear degeneration" of isolated areas of the upper epidermis, a phenomenon quite distinct from parenchymatous edema.

TAUSSIG, San Francisco.

CHRONIC MILIARY TUBERCULOSIS. GUNTHER ELIAS, Monatschr. f. Kinderh. **49**: 397 (March) 1931.

Two cases of miliary tuberculosis in infants are reported which ran a chronic course, one of four months and the other of a year. Roentgenograms are shown. Only six such cases have been previously reported.

GERSTLEY, Chicago.

TUBERCULOUS MENINGITIS. OSCAR HERTZ, Monatschr. f. Kinderh. **50**:237 (July) 1931.

Symptoms suggestive of tuberculous meningitis are vomiting and dermographia. Add to this a clear spinal fluid with an increased cell count and a positive Pandy test, and only encephalitis and aseptic meningitis need be ruled out. The incidence of the disease is characterized by a definite peak in April and May. Contrary to general impressions an intrafamilial infection could be demonstrated in only 37 per cent of cases. Again contrary to popular conception, neither measles,

whooping cough nor chickenpox seemed to have any influence on the frequency of tuberculous infection. Of much greater importance, the author believes, is the uncontrolled employment of ultraviolet irradiation. Especially is this true in pale blond children. Hertz definitely believes that he has seen seven cases of tuberculosis become active following treatments for only several minutes with ultraviolet rays.

While a few of his sixty-four patients entered the hospital in a state of good nutrition, most of them were undernourished. Breast feeding did not seem to offer any protection. The duration of the disease averaged twenty-three days. The white count need not be increased, but there is a characteristic relative and steady increase in the granulocytes without any decided increase in the toxic granules. The prevention of tuberculous meningitis is the same as that of tuberculosis with regard to hygiene of the home, routine physical examinations and the segregation of infected persons.

GERSTLEY, Chicago.

RESULTS OF ANTITUBERCULOUS VACCINATION BY THE CALMETTE METHOD IN WARSAW, POLAND. PROKOPOWICZ WIERZBOWSKA, Pedjat. Polska **10**:1 (Jan.-Feb.) 1930.

Between 1926 and 1929, 3,640 infants were vaccinated against tuberculosis, with the following results: 1. No ill effects on the develoment of the children were noticed. 2. External factors, like poor hygiene, malnutrition, contagious disease, gastro-intestinal disturbance and upper respiratory infection, did not increase the incidence of tuberculosis among the children vaccinated with B C G. 3. Children dying from other causes did not show tuberculosis at autopsy. 4. Sixty-five per cent of the vaccinated children in the tuberculous area showed tuberculosis, but the process was not active in all cases; if it became active, it was of mild form. Experimentation with these children is still going on, and sufficient data cannot be given at present. 5. The Pirquet test was mildly positive in 23 per cent of vaccinated children. 6. Isolation of all vaccinated children for a period, as advised by Calmette, is indispensable.

KRUPINSKI, Chicago.

Internal Diseases

LATE EFFECTS OF TREATMENT OF THYMUS. JOHN M. BARNES, Am. J. Roentgenol. **22**:220 (Sept.) 1929.

Sixty-three children who had received treatment for enlarged thymus were studied through questionnaires based mostly on the opinions of physicians. These children after from three and a half to eight years presented no constant deviation from normal in either the physical or the mental sphere, which might be attributable to the treatment, even though the dosage was somewhat high in the light of present knowledge.

STULIK, Chicago.

THE SIGNIFICANCE OF CALCIFIED ABDOMINAL LYMPH NODES. ROSS GOLDEN and ROBERT J. REEVES, Am. J. Roentgenol. **22**:305 (Oct.) 1929.

Calcified glands are more often due to tuberculosis, less often to typhoid fever and rarely to parasitic infection. Various authors cite as many as 1.7 per cent with calcified abdominal glands in children giving positive reactions to tuberculin. The differential diagnosis includes acute and chronic appendicitis, gallbladder disease, urinary tract stone or peptic ulcer. The sequelae are: (1) adhesions, (2) pressure on adjacent structures, (3) perforation of caseous glands into the peritoneum and (4) generalized miliary tuberculosis. The suggested terminology is tuberculous mesenteric lymphadenitis or calcified tuberculous mesenteric lymphadenitis. Only calcified glands can be diagnosed with the roentgen rays, and then not when superimposed on the spine. In the latter case the glands may be found in the lateral exposures. The irregular outline of the shadow differ-

entiates the gland from kidney stone, which is usually of homogeneous density. Surgical excision is recommended in selected cases. Case reports and a bibliography are included.

STULIK, Chicago.

ACUTE PULMONARY EDEMA OF ANAPHYLACTIC SHOCK: A CASE REPORT WITH ROENTGEN FINDINGS. H. F. DAY, W. R. SISSON and E. C. VOGT, Am. J. Roentgenol. **22**:349 (Oct.) 1929.

A boy of 14 years developed edema of the lungs about a half hour after the intramuscular injection of 1,500 units of antitetanic serum and after gas-ether anesthesia for a minor injury. The first film taken immediately after the subsidence of acute symptoms revealed a diffuse pulmonary congestion. In twenty-four hours a marked clearing occurred, and after seventy-two hours no deviation was discernible. A week after injection a moderate attack of urticaria was controlled by epinephrine. During the acute attack atrophine, morphine and oxygen were used.

STULIK, Chicago.

THE PROGNOSIS OF ACUTE GLOMERULAR NEPHRITIS IN CHILDHOOD. HARRIET G. GUILD, Bull. Johns Hopkins Hosp. **48**:193 (April) 1931.

From 1912 to 1928, 180 cases of acute glomerular nephritis were on record in the Harriet Lane Home. Of these patients, 28 died, a total mortality of 15 per cent, but only 6 deaths were due to nephritis, an actual mortality of 3.33 per cent. Thirty-four cases were followed from one to twelve years (18 less than five years, and 16 more than five years, after the nephritis). Careful interval histories were taken; complete physical examinations and the following tests were made: urinalysis, tests for kidney function, chemical analysis of the blood, phenolsulphonphthalein excretion and concentration tests. All except one girl with advanced rheumatic heart disease were symptomatically well with no impairment of kidney function. Nine cases showed albuminuria; 3 of these were orthostatic and 1 was due to cardiac decompensation, so that the persistent albuminuria could be attributed to nephritis in only 5. Fifteen of the normal patients passed through subsequent infection including scarlet fever and erysipelas without a recurrence of the nephritis. All but 6 of the patients were 7 years of age or less at the time of the nephritis. The percentage of these patients now showing albuminuria is definitely less than the percentage of those in whom the nephritis occurred at an age beyond 7. The severity of the nephritis and duration of stay in the hospital did not influence the prognosis. Although many of the patients are now entirely normal in spite of the neglect of foci of infection following the attack of nephritis, the fact that several of those now showing some abnormality are among those neglected makes one feel that it is wise to attend to such foci promptly in all cases.

LYTTLE, New York.

COMPLICATIONS INCIDENT TO INACCURATE OR DELAYED DIAGNOSIS IN SUPPURATION OF THE LUNGS AND PLEURA. WILLIAM L. KELLER, Bull. New York Acad. Med. **7**:202 (March) 1931.

Early diagnosis based on a painstaking history and careful physical examination (dulness, diminished or absent tactile fremitus and diminished breath sounds), followed by roentgen examination and aspiration at the point of greatest dulness, are of the greatest importance in influencing the mortality and morbidity of empyema.

In the acute stage it is necessary to determine the type of causative organism. The hemolytic streptococcus tends to produce a low vital capacity. Surgical intervention in this type of empyema is most dangerous. Collapse (a sudden change from normal negative intrathoracic pressure to abnormal atmospheric pressure) is a frequent complication. In pneumococcus empyema the fluid is rich in fibrin and insures early adhesion of the pleural surface, stabilizing the

intrathoracic viscera, and minimizes the tendency to lung collapse. Tuberculous empyema can be diagnosed from the history: the previous existence of pleurisy or tuberculosis of the lungs or other organs. The empyema is a form of suppurative pleuritis in which the tubercle bacillus is the only etiologic factor, but often invasion by this organism produces a mixed infection. The greatest tragedy that can befall the patient with tuberculous empyema showing a sterile exudate in the chest cavity is to subject him to an open thoracotomy. The element of contamination is always a menace to an already handicapped person (tuberculous).

Patients with chronic nontuberculous empyema should be treated by the many-stage open method. The mortality, in spite of the severe septic symptoms that many of these patients present (physical and mental depression, clubbed fingers, swollen joints, heart and kidney damage), is less than 9 per cent.

Acute lung abscess is seldom primary; it is usually associated with other chest conditions. About 1 per cent of the cases result from the presence of foreign bodies. Most of them are postoperative, following chiefly tonsillar and abdominal operations. The abscess may be parenchymatous or endobronchial, single or multiple. The single abscess is usually in the lower lobe and is more common in the right lung than in the left. In pneumonia the abscess begins in the area of consolidation. This is also true of abscesses resulting from septic emboli. Symptoms of the postoperative abscess may appear within twenty-four hours to one week after operation (e. g., respiratory embarrassment, cough with the sudden expulsion of large quantities of sputum or intermittent fever with chills).

The physical signs of lung abscess may not appear until after the cavity is evacuated (tympany, whispering pectoriloquy or amphoric breathing). The abscess may terminate by rupture into a bronchus or into the pleural cavity, or both. Adequate drainage (postural), with the patient free from irritation-inducing fulness, precipitating coughing spells, offers a favorable outcome of the condition if instituted immediately after the first productive coughing spell occurs, preceded by respiratory embarrassment, fever and leukocytosis.

JAHR, Omaha.

BACTERIOPHAGE AS A TREATMENT IN ACUTE MEDICAL AND SURGICAL INFECTIONS. F. D. HERELLE, Bull. New York Acad. Med. **7**:329 (May) 1931.

A scholarly yet practical discussion of the bacteriophage is presented, with the principles on which this work is based and a thorough review of the study of immunity leading to the discovery and preparation of the bacteriophage. This biologic element has proved efficacious in many bacterial diseases of the tropics, where it was first tried, and also in some of the diseases which are encountered in the northern countries. Some of the more familiar germs which have yielded this dissolving agent (bacteriophage) are *eberthella dysenteriae, paradysenteriae, typhi* and *parathyphosus, Sanguinaria, Escherichia coli, Salmonella schotmuelleri* and *suipestifer, Proteus vulgaris, Vibrio comma, Corynebacterium diphtheriae, Bacillus subtilis,* staphylococci, streptococci and pneumococci. From the diversity of the bacteria attacked, the author believes that the dissolution phenomenon is general, perhaps, for all bacteria.

Numerous incidents are cited in which the bacteriophage was used in various epidemics with remarkably favorable results. Bacteriophage therapy, the author concludes, is still in its infancy, and many studies are yet necessary before one learns all the results that may be anticipated, but what has already been done in many diseases justifies the belief that this is the treatment par excellence and that it will attain a wider and wider application.

JAHR, Omaha.

PNEUMONIA IN CHILDREN. E. EARL MOODY, California & West. Med. **34**:340 (May) 1931.

The author's abstract is as follows: "1. It pays to give good care to children in building up their resistance against infections with proper hygiene, good food

and proper inheritance. 2. Early hospitalization will lower the death rate to a marked degree. 3. The death rate in pneumonia in children is probably slightly lower here (Los Angeles) than in other sections of the country with a less favorable climate. 4. An accurate diagnosis in pneumonia, even with the aid of the x-ray, is still a difficult and uncertain procedure."

DICKEY, San Francisco.

THE ASSOCIATION OF DIABETES INSIPIDUS AND DIABETES MELLITUS. FRANK N. ALLAN and LEONARD G. ROWNTREE, Endocrinology **15**:97 (March-April) 1931.

After a review of the reports found in the literature of the coexistence of glycosuria and diabetes insipidus in a patient, Allan and Rowntree record three cases of this association. One of these was in a boy of 14 years. The diagnosis of both diabetes mellitus and diabetes insipidus was well established. The diabetes insipidus had its onset at the age of 11, following an attack of encephalitis; three and one-half years later, a sudden loss of weight and strength associated with a sudden increase in polydipsia and polyuria apparently marked the onset of the diabetes mellitus. Examination disclosed signs of hypopituitarism: failure of growth, genital hypoplasia, obesity and a subnormal metabolic rate. Treatment by means of insulin readily controlled the glycosuria, hyperglycemia and ketosis, but did not affect the polyuria. Solution of pituitary given twice in twenty-four hours reduced the output of urine immediately from 9,800 to 1,850 cc. Neither drug interfered with the action of the other.

That the total number of authentic cases of the association of diabetes insipidus and mellitus is perhaps no greater than might result from pure coincidence is admitted, but a possible intimate relationship is suggested. The same intracranial lesion, resulting from the encephalitis, may be responsible for both the polyuria and the glycosuria, the latter being due to inhibition of pancreatic activity by the central nervous system or by the pituitary gland.

JACOBSEN, Buffalo.

THE HEREDITARY FACTOR IN HYPERSENSITIVENESS. ANAPHYLAXIS AND ALLERGY. GEORGE W. BRAY, J. Allergy **2**:205 (May) 1931.

The mode, manner, nature and results of inheritance are fully discussed. The author inquired for asthma, hay fever, eczema, urticaria and migraine in 4,152 relatives of 200 children with asthma. His conclusions are: 1. One is not justified in endeavoring to explain the transmission of the allergic diathesis solely according to mendelian laws as two modes appear to be involved: (*a*) germinal, or true mendelian transmission through the germ plasm of the parents; (*b*) placental or serum sensitization, not truly hereditary, being an active or passive fetal sensitization in utero. Statistical surveys have shown merely that the majority of allergies have one or more antecedents with some type of allergic manifestation, and that a certain proportion of children of allergic parents will develop manifestations. Other of these children, while not manifesting any sensitivity. themselves, may again transmit the tendency to their children. 2. In comparing the influence of the hereditary factor in anaphylaxis of animals with that of allergy in man, the two appear diametrically opposite; germinal transmission has not been reported in animals, but is frequent in man; active sensitization in utero is difficult in animals but possible in man; passive sensitization is the common mode in animals but rare in man. 3. From the author's own observations it would appear that: (*a*) The greater or more complete the inheritance, the earlier the age at which symptoms will have their onset; this is confirmed even during the first decade, for when the inheritance is bilateral, practically all cases have had their onset before the sixth year; when unilateral, before the eighth year, while children with a negative history are not affected before puberty. (*b*) The diathesis is transmitted twice as often through the mother as through the father, and twice as many offspring are likely to be

affected when the female transmits. Of the offspring, over twice as many males as females are likely to be affected before puberty; the probability of recovery at puberty is much greater in the boy than in the girl, and the chance of developing allergic manifestations after that age is more probable in the female than in the male. (*c*) A positive family history was determined in 68.5 per cent of cases; in 51.5 per cent the condition was unilateral and in 17 per cent bilateral. 4. There is no positive proof that the distinctly familial types of angioneurotic edema, migraine, ichthyosis or, in the author's experience, epilepsy, are of an allergic nature. 5. The nature of the allergic diathesis would appear to be that of a particular biochemical make-up, a tendency to store up much alkali reserve without becoming definitely alkalotic. 6. The greater or more complete the hereditary influences are: (*a*) the earlier the age at which symptoms will have their onset, (*b*) the more frequent are skin reactions showing positivity and multisensitivity, (*c*) the greater the number of manifestations, (*d*) the greater the number of progeny affected, and (*e*) the more likely are the progeny to show the same allergic manifestation as the parents.

HOYER, Cincinnati.

A COMPARISON OF RAGWEED POLLEN INCIDENCE IN THE UNITED STATES FOR 1929 AND 1930. O. C. DURHAM, J. Allergy **2**:258 (May) 1931.

There is a ragweed map showing the comparative pollen concentration in thirty cities in the United States and four in Canada. A number of figures and tables show the comparative curves of pollen concentration, wind movement, rainfall and sunshine in these cities. The author's conclusions are: 1. A northern boundary of the effective ragweed area is suggested. This includes the agricultural districts of Quebec and Toronto but very little of central Canada. 2. Low pollen concentration in Toronto is accounted for by the phenomenon of "land and sea" breezes. 3. Florida is practically free from ragweed pollen. 4. The severe drought of 1930 reduced the United States ragweed pollen crop 43 per cent below the figure of 1929. 5. July seems to be the critical month for the development of ragweed. 6. The greatest effect of the drought was on giant ragweed. 7. Apparently the weather factors that produce a poor corn crop likewise produce a poor ragweed crop.

HOYER, Cincinnati.

UNDULANT FEVER IN A CHILD UNDER SEVEN MONTHS OF AGE. OLIVER W. HILL and RALPH H. MONGER, J. A. M. A. **97**:176 (July 18) 1931.

In an infant aged 7 months, almost entirely breast-fed save for an occasional sip of pasteurized milk, undulant fever developed as confirmed by the agglutination tests. The infant seemed to respond to the administration of paternal blood. Studies on the mother's milk were not possible.

BONAR, Salt Lake City.

PYURIA AND URINARY TRACT ABNORMALITIES IN CHILDREN. HOWARD REID CRAIG, M. Clin. North America **14**:1483 (May) 1931.

After detailing a number of very interesting cases, the author disclaims any intention of suggesting that most or even a large proportion of cases of pyuria are due to structural abnormalities. These conditions are sufficiently common, however, to demand of the physician the use of every urologic diagnostic measure in cases which do not yield to the usual medical treatment after a reasonable trial. The usual case of pyuria, in reality probably a pyelonephritis, commonly follows an upper air passage infection and usually is a self-limited condition, best treated by rest in bed, forcing fluids, colonic irrigation and alkalis. Experience with urinary antiseptics has not been satisfactory.

A striking thing about patients presenting congenital abnormalities is that while the condition has persisted from birth, in many instances the children go on for months or years without symptoms. The condition becomes manifest when, following infection elsewhere in the body, localization occurs in the kidney

with resultant pyelonephritis. On account of the abnormality, drainage is poor, and the pyuria once set up, becomes permanent unless suitable drainage is established. Vaccines have been of little benefit. Treatment of obvious purulent foci sometimes gives excellent results. The clearing up of infection in the paranasal sinuses has been more satisfactory than measures directed toward the tonsils. Surgical measures should be resorted to when necessary and feasible.

SMITH, Ogden, Utah.

THE CLINICAL SIGNIFICANCE OF ABDOMINAL PAIN IN CHILDREN. EDWARD J. WYNKOOP, New York State J. Med. **31**:86 (Jan. 16) 1931.

Delay in making a diagnosis in abdominal conditions frequently causes serious results. The author urges that the history be carefully studied and that the physical examination be made with great care. Too much dependence may be put on the blood count and on the roentgenogram. One must depend more on touch and hearing.

AIKMAN, Rochester, N. Y.

CONGENITAL CAPILLARY ANGIOMA OF THE PAROTID GLAND. M. J. FEIN, New York State J. Med. **31**:340 (March 15) 1931.

A child, 8 months of age, had shown since birth a swelling over the right parotid region. The mother noticed that the tumor increased in size when the child cried. The skin over the tumor was smooth, freely movable and not discolored. No pulsation was present. The tumor was easily removed and results have been good for three years. The tumor measured 5 by 3 cm. and proved, on microscopic examination, to be a capillary angioma of the parotid gland. Eight similar cases were found in the literature.

AIKMAN, Rochester, N. Y.

LOBAR PNEUMONIA COMPLICATED BY ATELECTASIS IN A CHILD WITH COMPLETE SITUS INVERSUS. MORRIS GLEICH, New York State J. Med. **31**:684 (June 1) 1931.

The cause of the atelectasis in this case was not determined. It was thought to be due either to a mucous plug in a bronchus or to the abnormal position of the heart. The child, 7 years of age, made a good recovery.

AIKMAN, Rochester, N. Y.

GINGIVITIS: VIII. GINGIVITIS AN ENTITY, INCLUDING ALL FORMS FROM ACUTE VINCENT'S TO CHRONIC PYORRHEA: DESCRIPTION, BACTERIOLOGY AND PATHOLOGY. ROBERT A. KEILTY, South. M. J. **24**:384 (May) 1931.

The author calls attention to gingivitis infection. All inflammations about the teeth, not otherwise specific, have been classified as acute and chronic gingivitis. Bacterial flora and the protozoal infestations are offered as the most important etiologic factors; all other factors are of but secondary importance. *Protozoa,* spirilliform organisms and streptococci may be the predominant forms of organisms in the acute type of gingivitis. In the chronic forms of gingivitis there is a wide variety of bacteria and *Protozoa:* the spirilliform group, *Fusiformis, Vibrio* and *Leptothrix* which are found on smear with the protozoal *Entameba* and *Trichomonas.* Occasionally diphtheria bacilli, Vincent's organisms or streptococci are found.

The author proposes a method by which he can rapidly pick out in vitro an antiseptic substance which might act as a specific in vivo. This procedure he designates as elective bacteriostasis. He believes it is of considerable clinical value. According to the author, the study has established the fact that preoperative gingival treatment has eliminated postoperative infection with cellulitis, osteomyelitis and death.

SCHLUTZ, Chicago.

THE PERIODICAL SEASONAL INCIDENCE OF GASTRO-INTESTINAL SYMPTOMS COMPLICATING RESPIRATORY INFECTIONS IN CHILDHOOD: SEASONAL GASTRO-ENTERITIS. C. C. MCLEAN, South. M. J. **24**:624 (July) 1931.

In an analysis of 235 patients with gastro-intestinal symptoms seen in private practice by the author, it was found that approximately 60 per cent were associated with a respiratory infection. The most characteristic symptoms were either nausea, vomiting or paroxysmal abdominal pains. There were drowsiness, dehydration and embarrassment of respiration. Prostration was out of proportion to the apparent illness of the child. During the first twenty-four hours of the illness the urine invariably showed a heavy acetone reaction, and the increase in the neutrophilic percentage was out of proportion to the increase in the number of white blood cells. The condition appears to be a seasonal disease; a larger percentage of the cases were seen during the months of January and February. The condition is evidently a definite entity. The gastro-intestinal symptoms are probably caused by some unknown specific toxin or virus associated with the disease, acting directly or indirectly on the alimentary tract. The cases reported have the characteristic signs and symptoms of so-called alimentary or intestinal intoxication.

SCHLUTZ, Chicago.

PYELITIS IN CHILDREN. W. B. REEVES, Texas State J. Med. **27**:18 (May) 1931.

Alertness in recognizing the condition and avoidance of instrumentation in diagnosing and treating sick children were stressed by the author. The treatment used was the changing of the reaction of the urine. First, sodium citrate was given in 10 grain (0.648 Gm.) doses every four hours and well diluted with water to a child 10 years of age. The urine was alkalinized in from forty-eight to seventy-two hours. After alkalinity had remained for a few hours, as tested with litmus paper, the alkaline treatment was stopped, and 5 grains (0.324 Gm.) of acid sodium phosphate with 10 grains of iopax, well diluted in water, was given every four to six hours. Irrigation of the bladder and other instrumentation was condemned.

MOORE, Dallas, Texas.

ON ENURESIS. LEOPOLD MANDEL, Brit. J. Child. Dis. **28**:1 (Jan.-March) 1931.

The author's summary is as follows: "Enuretics are classified into five groups to make them clinically more easily recognized: 1. Those in which some palpable physical irritating stimuli exist—worms, overdistention of bladder, cystitis, etc. The treatment is obvious. 2. The hypersensitive, neuropathic or nervous type, in which the instability is a symptom which may be regarded in the same light as other symptoms, such as cyclic vomiting, ketonuria, vagotonia, etc., which are commonly found in the nervous child. They respond to dietetic and medicinal measures combined with readjustment of environment and gentle education. 3. The so-called psychopathic child, in whom the enuresis is more a behaviour complex and the treatment is for the most part psychological. 4. Endocrine disharmony, particularly hypothyroidism, leads to a loss of inhibition. Giving thyroid in small doses is indicated, whilst pituitrin by its tonic effect on unstriped muscle is a good adjuvant. 5. The debilitated child, often convalescent from some illness. General tonic treatment is indicated.

In all cases atropine (and belladonna) is the specific drug of choice. In the management of the case the closest cooperation and patience between the doctor, the child, the parent and the teacher is essential."

LANGMANN, New York.

CARDIAC THROMBOSIS. L. MARCHADOUR and DUPIRE, Nourrisson **19**:98 (March) 1931.

Thrombosis of the left auricle is usually associated with mitral disease. Its primary development is much less common. The case described, occurring in an infant aged 18 months, is an example of this rarer form. The thrombosis was not suspected during life. The clinical picture was one of anemia, malnutrition, fever, a rapid pulse rate and an enlarged liver and spleen. Mild rickets and a slight generalized adenopathy completed the abnormal findings. Laboratory examination revealed a marked secondary anemia with leukocytes normal in number and formula. The blood cultures remained sterile. The tuberculin test was negative.

During the hospital residence a mild attack of diphtheria occurred, responding promptly to antitoxin. Bronchopneumonia hastened the unfavorable downhill course.

At autopsy in addition to foci of pneumonia in the lungs a large organized thrombus adherent to the interventricular septum was found in the left auricle. The heart was enlarged in volume, especially the left auricular appendage. This megacardia had not been recognized ante mortem. Roentgenograms showed no increase in the size of shadows at the hilus. The size of the heart shadow is not mentioned.

McCLELLAND, Cleveland.

TRANSITORY ANOMALIES OF THE CARDIAC MECHANISM. E. GERAUDEL and D. GOMEZ, Paris méd. **1**:256 (March 14) 1931.

A girl, aged 10 years, suffered with cardiac insufficiency for six months, following rheumatism. The electrocardiogram showed some variations of mechanism. The P-R interval was lengthened, although irregularly so, and there was a sinu-auricular block, as well as ventricular and auricular arrhythmia. These anomalies were exaggerated by ouabain (0.125 mg. intravenously every six hours), which revealed the latent condition.

SANFORD, Chicago.

CHRONIC ENDOCARDITIS IN A CHILD. PAOLO IACCHIA, Pediatria **39**:603 (June 1) 1931.

The author reports a case of chronic endocarditis due to invasion by Streptococcus viridans, with isolation of the organism, in a child 5½ years of age. The duration of the disease was three years and five months, at which time the child died. During the course of the disease emboli were observed in the spleen, lungs and left sylvian artery. The case is of interest because of the unusually long duration of the disease, and statistically because the patient is among the youngest so far reported.

SIGNORELLI, New Orleans.

CLINICO-ANATOMIC CONTRIBUTION ON THE RECOGNITION OF OSTEOGENESIS IMPERFECTA. CATELLO SORRENTINO, Pediatria **39**:625 (June 15) 1931.

The author reports a case of "osteogenesis imperfecta" in an infant 5 days old. He presents in detail the clinical and anatomic observations, as well as a complete roentgen study of all bone changes at various intervals during the course of the disease until the death of the patient at the age of 6½ months.

SIGNORELLI, New Orleans.

VULVOVAGINITIS IN INFANTS. GUIDO GUGLIELMINI, Prat. pediat. **9**:65 (Feb.) 1931.

Guglielmini briefly reviews the etiology, symptomatology, diagnosis, course, complications, prophylaxis and treatment of gonorrheal vulvovaginitis. After listing a great variety of local treatments, he concludes that success depends more

on the diligence with which the treatment is performed than on any particular method. He recommends vaccines only when there is coexisting arthritis. He seems convinced that numerous patients are condemned to sterility by this disease.

DOOLEY, Kent, Conn.

ACTION OF THYMUS PREPARATION ON THE DESCENT OF THE TESTES. C. I. PARHON and H. ELIAS, Med. de los niños **32**:16 (Jan.) 1931.

The testes may be surrounded by adipose tissue which prevents the normal descent. This tissue is absorbed by means of thymus extract.

DWYER, Kansas City, Mo.

THE THYMUS. BARLOLOMI PLA, Med. de los niños **32**:101 (April) 1931.

The author discusses briefly the development and the anatomy of the thymus. The gland commences to atrophy after the fourteenth year. It is most active during the period of infancy, and exercises its principal action in the development of the osseous system.

DWYER, Kansas City, Mo.

ACTION OF VARIOUS PROTEINS ON BLOOD SUGAR (IN DIABETES). H. GLATZEL, Arch. f. exper. Path. u. Pharmakol. **143**:234, 1929.

In diabetes after the oral administration of protein, a strong tendency to hyperglycemia is obtained. The hyperglycemia after a single administration of 20 Gm. of dextrose by mouth to a diabetic patient after an egg-protein diet is less and lasts for a shorter time than that after a pure fat-vegetable diet. If the egg-protein be replaced by a corresponding amount of flesh-protein, the hyperglycemia is greater and lasts longer.

KUGELMASS, New York.

MILIARY LIVER NECROSIS IN INFANTS. W. IFF, Beitr. z. path. anat. u. z. allg. Path. **86**:83 (Jan. 3) 1931.

Miliary necrosis in infants occurs chiefly in the liver, although other organs may be affected. While most authors agree on the morphologic description of the causative organism, they disagree as to the etilogy of the pathologic condition. Some theories as to etiologic factors are: (1) an umbilical infection, according to Henle; (2) an enterogenous infection due to aspiration of vaginal secretion during birth, as suggested by Aschoff-Weede, Schneider, Frankel and Kantschewn; (3) alimentary intoxication, as held by Amsler and Konschegg, and (4) the presence of the pseudotubercle bacillus or (5) the pseudodiphtheria bacillus.

The author briefly describes cases quoted by other investigators and cites two of his own; in one of these a child was delivered two days after intra-uterine death due to premature separation of the placenta, which occurred one day before the rupture of the membranes. The lesions in the liver varied in size from 0.5 to 1 mm. in diameter and were confluent in some parts. They could be reproduced in laboratory animals. The author was unable to isolate the pseudodiphtheria bacillus, the pseudotubercle bacillus or similar organisms. He did, however, isolate a definite organism. Thus he discredited the theories as to the bacteriologic observations.

On the basis of his observations on the still-born infant, he disproves the theory of uterogenic and umbilical infection, but believes that the placenta is the source of infection. The mother has a certain amount of resistance and immunity to the organism, which may also be the case in infants who live for several weeks or months. Concerning the source of infection much is yet to be explained.

SCOBEY, Syracuse, N. Y.

INTRATHORACIC CYSTS. B. ENTZ and D. OROSZ, Frankfurt. Ztschr. f. Path. **40**:229, 1930.

In an infant, aged 11 months, a cyst was discovered in the thoracic cavity by the x-rays. The cyst was removed, but the child died eighteen days after the operation. The cyst occupied the larger part of the right thoracic cavity, extending from the fourth rib to the diaphragm. It was covered by a smooth and glistening pleura, and was adherent to the thoracic wall and to the mediastinum. The adhesions were separated with ease. The cyst was not attached to the esophagus, trachea or thoracic duct. It could easily be removed from the underlying diaphragm. There was no connection between the cyst and any of the abdominal organs. The cyst measured 2 by 7 by 10 cm. The thickness of its wall varied to 6 mm. The content of the cyst, when first obtained by thoracentesis, was a clear yellow and somewhat mucinous, sterile liquid. A few leukocytes, lymphocytes, red blood corpuscles and degenerated epithelial cells were found in the sediment. Neither succinic acid nor scolices could be detected. The content of the cyst subsequently became turbid and, later, purulent. Histologically, the wall of the cyst revealed structures that were identical with gastric mucosa and muscularis. The authors believe that the cyst arose from a heterotopic island of gastric mucosa in the esophagus. After obliteration of the ducts of glands in such a heterotopic island, cysts may be formed which later lose their connection with the esophagus. According to Lauche, such cysts should be classified as choristoma.

[ARCH. PATH.].

RUPTURED ANEURYSM OF THE DUCTUS ARTERIOSUS. A. GUGGENHEIM, Frankfurt. Ztschr. f. Path. **40**:436, 1930.

A case of ruptured aneurysm is reported in a girl 20 months of age. The aneurysm had ruptured into the lower lobe of the left lung and into the left pleural cavity. In addition, the case revealed an empyema of the left knee joint. Histologically, the ductus arteriosus in the region of the rupture revealed a hemorrhage of the intima in several places. The intima was thickened, and the media markedly fibrosed. The point of rupture could be demonstrated in an area 2 mm. distant from the aorta. The author states that, on account of the empyema of the knee joint, it is possible that this is a case of mycotic aneurysm, even though the inflammatory changes in the wall of the ductus arteriosus were very slight. Streptococci could be cultivated from the pus of the knee and from the spleen.

SAPHIR, Chicago [ARCH. PATH.].

STATISTICAL STUDY OF PNEUMONIA IN CHILDREN. JULIUS LUCAS, Gesundhfürs. f. d. Kindesalt. **6**:93 (April) 1931.

The article does not bring out anything new. It is a statistical treatment of the cases of pneumonia seen in the Children's Hospital at Düsseldorf.

REICHLE, Cleveland.

ORAL DESENSITIZATION IN ALLERGIC DERMATOSES BY SPECIFIC PEPTONE. ERIC URBACH, Klin. Wchnschr. **9**:2046 (Nov. 1) 1930.

Alimentary idiosyncrasies may cause not only acute toxic exanthems but also the more chronic urticaria, prurigo, lichen urticatus and strophulus infantum. Epicutaneous and intracutaneous tests are often unsatisfactory. Better diagnostic results are frequently obtained with experimental food tests. One may begin with almost a starvation diet, consisting of tea, coffee, whisky (from 80 to 100 Gm.) and sugar for two days. After the urticaria clears up, other foods are slowly and systematically added, one at a time, beginning with butter, potato, fruit juice and leafy vegetables; then the chief animal proteins are added. After the reacting food is found, it is desirable to repeat the test and to see whether more than one

food substance is at fault. Occasionally the method of preparation of the food may cause the allergy, as in the case of a patient who reacted to omelet but not to boiled egg.

The intolerance may be overcome by (1) omitting the food from the diet, (2) omitting every kind of protein for fourteen days and then beginning with small amounts (this is particularly suitable for recently developed allergy), (3) exceedingly slow desensitization and (4) specific peptone therapy. The specific peptone therapy is based on skeptoprophylaxis, which consists in giving the offending food or medicament, in minute amounts, one hour before the ingestion of larger amounts of the same substance.

The best results, the author claims, have been obtained with specific peptones made from such food, and he has had peptones prepared from egg, milk, beef, pork, lamb, fish, corn, wheat, beans and peas. One-tenth gram is given from three-fourths to one hour before a meal containing the allergic food, beginning with small amounts. The time for desensitization by this method varies, but often fourteen days are enough to give permanent relief. In infants it becomes necessary to reduce the feedings to three or four per day, so that peptone will not be given while the stomach still contains food. For the same reason, nothing but water is given between meals.

SILVERMAN, Syracuse, N. Y.

ANIMAL STUDIES IN THE PATHOGENESIS OF CELIAC DISEASE. R. FREISE and E. WALENTA, Monatschr. f. Kinderh. **50**:1 (May) 1931.

The term celiac disease was first used in 1888, by Gee. It is a disturbance of nutrition affecting children at the end of the first and the beginning of the second year. The weight curve begins to descend. Even the height remains stationary. The physical strength diminishes, so that if the child has been able to walk he loses this power. Characteristically the abdomen is very large, and the facial expression that of senility. The stools are of particular interest, being increased in number, very large, foul smelling and often foamy. The theories concerning this disease are: (1) that it is a disturbance of the nervous regulation of the intestinal functions; (2) that it has to do with the intestinal flora, perhaps even a persistence of the gram-positive flora of early infancy.

Freise and Jahr were able to show, some years ago, that there was a marked increase in intestinal motility, food often passing the intestinal tract in from one to two hours. The authors used the fluoroscope to elaborate these studies and found that the food passed the entire small intestine within one-half hour. It passed the first part of the large intestine very rapidly, and it was only in the distal part of the large intestine that the rate appeared normal. The authors conclude that there is either a diminution in the inhibition exerted by the splanchnic nerve or an increase in the activity of the vagus.

They were not able to confirm this hypothesis by the use of atropine, but they did get a striking improvement in the clinical picture following the administration of opium derivatives. To confirm this theory further they sectioned the splanchnic nerve in young pigs. The stools at once increased in volume and, in respect to total nitrogen, fat, ash and water, took on the appearance of the stools in celiac disease. In addition, the animals lost weight and developed the same type of protuberant abdomen as in the clinical picture in infants. The authors conclude that section of the celiac plexus in pigs gives a picture much like celiac disease in human infants.

GERSTLEY, Chicago.

SPONTANEOUS FRACTURE IN A CHILD WITH LYMPHATIC LEUKEMIA. M. TRUSEN, Monatschr. f. Kinderh. **50**:45 (May) 1931.

The author presents a report and roentgenograms of a 5½ year old boy suffering from lymphatic leukemia. Apparently the excuse for reporting the case is that the patient had a spontaneous fracture of the left femur due to leukemic infiltration of the bone.

GERSTLEY, Chicago.

INDICANURIA IN NURSLINGS. H. PLONSKER, Monatschr. f. Kinderh. **50**:169 (June) 1931.

Half of the artificially fed infants studied (1,700 examinations in over 200 children) showed indicanuria. The occurrence did not depend on any constant factor, but seemed induced at times by infections and at times by diarrhea. On the other hand, of 6 children who were made constipated by opium used therapeutically, only 3 showed indican in the urine. Adding protein and fat to the diet did not produce constant results. The author falls back on the time-honored explanation of "constitution." Increasing the carbohydrate in the diet at times worked beneficially, and complete hunger often cleared the substance from the urine. The only infallible remedy was placing the children on diets exclusively of 15 per cent sugar solution. In 12 children this treatment was effective in from one to three days, but the indican returned with a resumption of the old diet.

GERSTLEY, Chicago.

HEMORRHAGIC DIATHESES. M. B. SCHMIDT, Verhandl. d. deutsch. path. Gesellsch. **25**:10, 1930.

In the main, the author concludes from an anatomic and experimental study that many of the conditions grouped under "hemorrhagic diathesis" may be explained by changes in the vascular walls, especially those of the venules. He urges that in the study of these conditions more attention be paid to the blood vessels. In his consideration of the various hemorrhagic diatheses he reaches the following conclusions:

Hemophilia.—No changes are found in the walls of the blood vessels. The possibility of chemical changes in the blood must be seriously considered. A similar picture is found in deep icterus and phosphorus poisoning, in which there is a disturbance of the formation of thrombokinase from injury to the liver. A clumping together of the thrombocytes in a slow circulation, without the formation of fibrin, causes an endothelial reaction that results in vascular rupture (Dietrich). This may explain the hemorrhages in hemophilia. One must not confuse this condition with pseudohemophilia, in which there is an absence of fibrinogen. This fact and the absence of a family history should exclude hemophilia vera.

Thrombocytopenia.—Thrombocytopenia may occur alone or secondary to infections or to diseases of the blood. That this condition is associated with thrombopenia does not mean that all hemorrhagic diatheses may be so explained. The cause of the thrombopenia, whether it is a decreased formation of platelets in the bone marrow (Frank) or an increased destruction in the spleen (Kaznelson), has not yet been determined. In a case of sudden generalized hemorrhage, the author found a mild infectious state of the blood vessels, especially of the small veins, with endothelial proliferation and perivascular round cell infiltration, but no bacteria. The bone marrow was normal, with no decrease in number or change of the megakaryocytes. From these observations the author concluded that there is no constant relationship between thrombopenia and hemorrhagic diathesis, and that the vascular changes are probably the most important factor.

Scurvy.—The deficiency of vitamins predisposes to infection by organisms already present in the skin, mouth, etc. In the skin the hemorrhages are about hair follicles because of infection there. The deep hemorrhages are also explained on an infectious basis, as the small veins show proliferation of the endothelium with perivascular round cell and leukocytic infiltration. Experimental scurvy in guinea-pigs shows similar histologic changes. Superimposed infection causes an increase in the hemorrhagic diathesis.

Panmyelophthisis (Aplastic Anemia).—Here, too, changes in the small veins are found where hemorrhages occur. In experimental benzene poisoning of rabbits hemorrhages were noted before the platelet count diminished, indicating that there is a toxic change in the wall of the blood vessels, and that the decrease in the number of platelets is not essential.

Schönlein-Henoch Purpura.—In this condition changes are found in the smaller blood vessels, similar to those described. The rôle of thrombi, as stressed by Silbermann, could not be verified. As it is difficult to reproduce a similar condition experimentally, little can be added.

Infectious Type.—Emboli of bacteria, as in meningococcic meningitis and bacterial endocarditis, and toxic changes of the endothelium, as in hemorrhagic smallpox, are the underlying factors in infectious conditions.

Uremia.—In uremia, a cytolysin is produced that dissolves the capillary endothelium as snake venom sacs.

ROSENTHAL, Chicago.

PROBLEMS CONCERNING ENURESIS. J. M. ESERSKY, A. I. PLOTITSCHER and A. M. FURMANOW, Ztschr. f. Kinderforsch. **38**:233 (March 12) 1931.

The article offers nothing new concerning the much discussed subject of enuresis.

REICHLE, Cleveland.

THE CAUSE OF CONVULSIONS IN SO-CALLED EKIRI, A CHARACTERISTIC DYSENTERY-LIKE INTOXICATION IN JAPANESE CHILDREN, VERY ACUTE AND SEVERE. H. HARA, Ztschr. f. Kinderh. **50**:520 (Feb.) 1931.

In so-called ekiri there is an increase in the permeability of the intestinal wall, proportional to the degree of intoxication. In this, as well as in similar diseases in which convulsions happen, the blood ammonia increases from seven to eleven times the normal amount. On the other hand, in other diseases accompanied by convulsions, no increase occurs, and in rabbits treated with poisons causing convulsions, like picrotoxin and strychnine, and in rabbits deprived of their epithelial corpuscles, the blood ammonia does not increase; nor is an increase of guanadine and methyl-guanadine observed. Between the convulsions and the increase in ammonia a causal relation must exist, and the abnormal increase is no secondary result of an injury to the central nervous system or the epithelial corpuscles. Because of the following facts in ekiri and experimental dysentery in rabbits, the disturbance of the capacity of the liver for the formation of urea, the decline of the capacity of the reticulo-endothelial cells for the storage of foreign bodies, the slowing of the time of excretion of santonin, the appearance of acetone, urobilinogen, urobilin and bilirubin in the urine and the slight increase of bilirubin in the serum, a disturbance of the function of the liver is to be assumed. The histologic changes are not marked, but one finds cloudy swelling and fatty degeneration of the liver cells, and also atrophy, when the intoxication has been severe, and death has followed. The swelling and increase of the reticulo-endothelial cells varies with the degree of intoxication. There is usually hyperemia. The fact that the lower edge of the liver varies during the course of the disease makes this change the more significant. Beside the increase in blood ammonia, there is a decrease of blood urea, a functional as well as an organic change.

Looking at these facts together, one has the following sequence: first, the liver cells are harmed by bacillary toxin absorbed from the intestine and portal vein, hence a disturbance of function, hence the diminished capacity for detoxification, hence the failure of ammonia to be changed into urea, hence the increase of ammonia in the blood and hence the convulsions. Whether the chief cause of the convulsions is ammonia alone, toxin or ammonia acting with toxin, Hara is not sure. Recently K. Meta has attempted to ascribe the cause to spasm of the cerebral vessels, and Hara has no ground for denying it. Some more work must be done on the mode of action of ammonia.

EMERSON, Boston.

NEW VIEWS ON SO-CALLED PYLORIC STENOSIS. W. LEHMANN, Ztschr. f. Kinderh. **50**:691 (March) 1931.

Tumor of the pylorus is to be looked on as an acquired, compensatory hypertrophy of the muscle in a congenital, functional blockade. Pyloric stenosis, with

vomiting, increased peristalsis and constipation, comes to pass if the summation of peripheral stimulation caused by forced contractions of the stomach leads to overirritability of the vagus center. The changes frequently observed in the esophagus, large intestine and urogenital system in association with pyloric stenosis are not to be taken as malformations, for they are due to functional closure of the sphincters, leading to hypertrophy and dilatation of the organs concerned, e. g., cardiospasm, Hirschsprung's disease, congenital dilatation of the bladder, of the ureters and hydronephroses. How the pathologic outlet, or the congenital failure of the reflexes for opening the sphincters, is caused is as unexplained as the peculiar inheritance that is expressed in pyloric stenosis in boys. By the aid of conservative methods one can eliminate only the neurogenous component engrafted on the primary disease, the stenosis and hypertrophy of the muscle remaining unchanged. This explains the persistence of the tumor, despite clinical treatment. The excellent results of the Weber-Rammstedt operation, which is the only justifiable operative procedure, rest less on the cleavage of the musculature of the canal than on that of the pyloric ring. The mortality of this operation, though increased by unsuitable cases, is less than that of conservative treatment. The fatal cases are due only in part to the operation. They are avoidable and must be avoided if the operation is to be saved from falling into discredit. In each case, conservative treatment must first be tried, but if the weight continues to fall under experienced pediatric treatment for six or eight days, the operation must not be delayed, after which the infant should immediately be returned to the pediatrician.

EMERSON, Boston.

ANATOMIC CONDITIONS PRELIMINARY TO INFANTILE PYLORIC STENOSIS. A. DIETRICH, Ztschr. f. Kinderh. **50**:705 (March) 1931.

The relation of the pylorus to the liver, which is determined by the ligamentum hepatoduodenale, shows great variations which may be divided into two groups. (*A*) The duodenum is so attached to the liver that it describes a flat curve, and after the stomach is filled, there is but little emptying through the pylorus. (*B*) The region near the pylorus is so attached that it is drawn to the liver, and after the stomach is filled, the duodenum is kinked. In this group there are many stomachs with a strong pars pylorica; there are stomachs with a distinct hypertrophy but with no clinical signs of stenosis, and there are undeveloped forms that are accompanied only by disturbances of digestion, without spasm and vomiting. A third group (*C*) is made up of those stomachs which have a pronounced pyloric stenosis. The ligamentum is attached higher on the pylorus, as compared with group *B*, and grasps it or is attached laterally, and in drawing the stomach toward the liver, kinks the duodenum.

These anatomic conditions no not wholly explain the problem of infantile pyloric stenosis. To the change in position the setting up of the spasm must be due, and from this follows the hypertrophy of the muscle. The varying activity of both factors produces the difference, clinical and pathologico-anatomic, in each case.

Cleavage of the muscle by Rammstedt's operation removes the spasm, and gastric peristalsis is enabled to adapt itself to the conditions. The same thing can be accomplished by proper dietary treatment.

EMERSON, Boston.

ACID-BASE METABOLISM: THE INFLUENCE OF HYDROCHLORIC ACID IN DIABETES MELLITUS. H. FASOLD, Ztschr. f. Kinderh. **50**:715 (March) 1931.

To a diabetic child with healthy kidneys, a low blood chloride and considerable hyperglycemia, the chloride given in the form of hydrochloric acid was completely excreted. The sinking of the blood chloride was studied as a process compensatory to organic acidosis. Attention is drawn to the high degree of existing organic acidosis, 30 per cent of which was caused by ketone bodies; i. e., most of it was made up of other organic acids. In spite of the acidosis

an important amount of mineral base was excreted from the buffer system phosphoric acid-organic acid, as a regulatory means. Apparently this excretion of alkali occurred with the help of organic acids. After the giving of hydrochloric acid those bases bound to chlorine were excreted. At the same time the quantity of organic acids was considerably reduced. The exhibition of hydrochloric acid had no influence on the excretion of ketone bodies. This is referred to the diet used, and it is noted that in other alkaline diets, Falta's flour-fruit cure or Petrén's vegetable cure, a diminution of the ketone bodies may happen because in these diets a fraction of the ketone bodies serves to transport alkali.

EMERSON, Boston.

THE PANCREAS IN CHILDREN. O. KITAIGORODSKAJA, Ztschr. f. Kinderh. **50**: 748 (March) 1931.

The pancreas, like other organs, becomes diseased under the influence of various toxic and infectious agents, traumas, etc., and disease causes disturbances of function, diminution in the quantity of a secretion and the amount of ferments. In children an inadequate function of the pancreas is found with disturbances of nutrition which can be looked on as secondary. Doubtless, among children in their first year there exists a group of hypotrophics, as a result of congenital malformations or inflammatory changes. There may be the greatest variety in the way in which this inadequacy is expressed: large stools with an increased content of fat, sugar in the urine, etc. The intensive dynamic study of the duodenal juice is important, which establishes what part of the function is disturbed. Organotherapy should unquestionably be used. Once the attention and interest of physicians is directed to the possibility, functional disturbances of the pancreas will be recognized much more frequently, and therapy will be directed to a known end.

EMERSON, Boston.

HYPOTHYREOSIS WITH RICKETS AND ANAEMIA PSEUDOLEUKAEMICA. W. STOELTZNER, Ztschr. f. Kinderh. **50**:785 (March) 1931.

A boy, 1 year and 10 months old, who had never been fed goat's milk or vegetables, was of a golden, pallid color from birth, and slept a great deal. Treatment with cod liver oil for three months did not make him improve. He was fat, had never sat up and showed many signs of rickets. The red blood cell count was 1,640,000, and the white cell count 9,300; the hemoglobin content was 20 per cent. Many normoblasts and some megaloblasts were present. He was given vegetables, fruit, cereal, liver and a transfusion of 96 cm. of blood. He improved rapidly for a time but now his condition remains the same; progress is hoped for again with a second transfusion.

EMERSON, Boston.

CASE OF NEPHROLITHIASIS IN A CHILD. K. HOMMA, J. Pediat. (Tokyo), June 20, 1931, no. 373, p. 773.

The author reports a case in a female child, 11 years and 10 months old, who had noted generalized vague pain over the back for three and one-half years. There was no history of frequent urination, hematuria or anuria. After admission, about seventeen small grain-sized soft stones were passed spontaneously, without pain on urination. Examination of the stones proved them to be of carbonate composition.

KATO, Chicago.

A CASE OF FATAL HEMORRHAGE FROM GASTRIC VARICES IN A BOY OF FOURTEEN YEARS. JOSEF LOSERT, Časop. lék. česk. **68**:491 (April 5) 1929.

A boy, aged 14 years, developed severe vomiting of blood associated with epigastric pain about twelve hours after lifting a heavy barrel. Vomiting persisted in spite of routine conservative treatment. Autopsy revealed no ulceration

of either the esophagus or the stomach, but several small varices were found along the fundus of the stomach. An organized thrombosis of the spleen was most likely the source of the varices, but the splenic vein was not examined to prove this. The conservative treatment was carried out because of the uniformly good results obtained, as, for instance, the 93 to 97 per cent recovery reported by Payr. In young children the varices are often considered as congenital or idiopathic and not ulcerous.

STULIK, Chicago.

Nervous Diseases

SYDENHAM'S CHOREA. R. W. WAGGONER, Am. J. M. Sc. **182**:467 (Oct.) 1931.

An interesting and brief historical sketch of Sydenham's chorea is given. It is essentially a disease of childhood, about 80 per cent of the cases occurring between the ages of 5 and 15 years. Females are affected twice as frequently as males. It is felt that such infections as acute rheumatic fever, acute tonsillitis, acute nephritis and scarlet fever are precipitating factors but not primary causes. The condition is characterized by moderately quick, irregular, spasmodic, jerky, uncontrollable muscular movements, associated with decreased tendon reflexes and practically always some mental symptoms in the acute stage. Pathologically it is a type of encephalitis characterized by both cortex and basal ganglion involvement.

The most essential points in treatment are complete physical and mental rest, sometimes best obtained by removing the patient from his present environment. The removal of foci of infection is important, but should be delayed until there has been a diminution in the movements exhibited, and until fever, should there be any, has subsided. The multiplicity of treatments suggested is partial evidence of their inadequacy.

HENSKE, Omaha.

THE TREATMENT OF POST-ENCEPHALITIC CHILDREN IN A HOSPITAL SCHOOL. EARL D. BOND and KENNETH E. APPEL, Am. J. Psychiat. **10**:815 (March) 1931.

The school for postencephalitic children was established at the Pennsylvania Hospital in 1926. The children admitted presented such behavior difficulties as lying, stealing, quarreling, enuresis, overaffectionateness, masturbation, swearing and cruelty. The nurse in charge of the school was psychiatrically trained, and could accept the irritating behavior of these children with equanimity and understanding. She took her meals with the children. Foster parents lived in intimate association with the children. In the school, recitation periods were short, but the children were kept busy almost all the time. A spirit of optimism was maintained, and the students were encouraged to feel that their difficulties were curable. Delinquencies were viewed unemotionally, and stress was laid on cooperation rather than on criticism, on understanding rather than on discipline. Twenty of the postencephalitic children were sent home, and seven showed a good social adjustment; of the forty-eight postencephalitic patients in the school, forty-five improved to a fair level. In addition to this improvement in the psychologic environment, the hospital, by rest, diet and hygiene in general has promoted physical repair.

DAVIDSON, Newark, N. J. [ARCH. NEUROL.].

THE TREATMENT OF CHOREA BY THE INDUCTION OF FEVER. LUCY PORTER SUTTON, J. A. M. A. **97**:299 (Aug. 1) 1931.

The author treated twenty-four patients with chorea minor by means of intravenous injections of typhoid-paratyphoid vaccine to produce fever. While the evaluation of any method of treating a disease as variable in severity and duration as chorea is difficult, the results so far have been good. There has been a prompt

cessation of symptoms and a shortening of the course. The average duration after treatment was started from eight to nine days. This treatment has been much more satisfactory than any other used and appears to have advantages over the use of phenylethylhydantoin.

BONAR, Salt Lake City.

THE CHILD OF VERY SUPERIOR INTELLIGENCE AS A SPECIAL PROBLEM IN SOCIAL ADJUSTMENT. LETA S. HOLLINGWORTH, Ment. Hyg. **15**:3 (Jan.) 1931.

The gifted child is more of a problem to himself and to his family than to society. There is a gap between his emotional stability and his intellectual status, and if he is placed in a grade in school to which his intelligence entitles him he is apt to be emotionally immature compared to his classmates; if placed in the grade corresponding to his age, he will find the work too easy and fall into idle day-dreaming. If he makes proper scholastic progress, he is obliged to associate with his duller seniors, and, being the youngest in his class, he is soon bullied and tormented by his older classmates. Gifted children are disinterested in the ordinary play of their contemporaries, and occupying the play time of these children presents a special problem. In the classroom they may become troublesome because they are able to express themselves and are unduly anxious to do so. It is unlikely that a really superior child will have parents both of whom exceed him in intellectual quotient, and this reversal of the usual relationship presents delicate problems in parent-child adjustment. The domestic management of these children is especially difficult, for they are quick to appreciate the types of behavior that bring them satisfaction. These gifted children are destined to be the captains of the future, and their training is of significance to society.

DAVIDSON, Newark, N. J.

MOTOR REEDUCATION IN BIRTH INJURIES. E. R. CARLSON, Yale J. Biol. & Med. **3**:411 (May) 1931.

The author presents the report of a case and the methods used in reeducation. He pleads for standardized methods of training these children, and concludes that when one considers all the waste among those who are not physically handicapped and who, in spite of educational resources, do not make good citizens, it does not seem unresourceful to devote more attention to those with cerebral birth palsy, many of whom with proper training might excel the average citizen.

SANFORD, Chicago.

SOCIAL PSYCHIATRY. D. K. HENDERSON, Edinburgh M. J. **38**:414 (July) 1931.

This is the third of the Morrison lectures for 1931, at the Royal College of Physicians, Edinburgh. Dr. Henderson is physician-superintendent of the Royal Mental Hospital and lecturer in psychiatry at Glasgow University. He believes that the public need is for the general practitioner to learn and practice psychiatry, so as to recognize early and guide into proper channels the numerous cases that occur.

A habit or nursery clinic for children under 5 years of age is a good beginning, for it will show whether the child is normal, or is suffering from disorders of conduct, either with or without proper intelligence. This permits the early establishment of guidance and training, thereby preventing nervous traits that would be difficult to stop in adult life. Child guidance clinics are conducted now not only for court delinquents, but for the prevention of problems that occur in the maladjusted child. The clinics should be connected with the educational system, the court and all charitable organizations, but especially with the hospital.

Henderson narrates the histories of eight children and six young adults, who had difficulties in social behavior and whose problems were straightened out in the outpatient psychiatric clinic. The older group showed more definite

delinquent tendencies. All patients coming to such a clinic can be helped in some degree. The author believes that one does not have to resort to intensive psychoanalytic methods in the outpatient clinic, but that one can use general psychotherapeutic methods. Children especially need only simple remedies, such as affiliation with an outside interest: a club or church or occupation in play or work. They need no "intrapsychic ponderings." For the necessary machinery a social service organization is indispensable for revealing the setting in which the patient's symptoms occur.

NEFF, Kansas City.

CONCUSSION AND MEMORY. C. W. SOMERVILLE, Tr. Med.-Chir. Soc., Edinburgh, 1930-1931; p. 121, in Edinburgh M. J., August, 1931.

Somerville relates his own history as a boy, when, after a fall from sliding down the banister, he could not remember the bump that he received. There was a hiatus, so that he could not remember the fall, but it did not affect his antecedent memory. As a medical student he had another fall, causing a hiatus in his memory. An acquaintance of the author was thrown from a horse, landing on his head, and was unconscious for a short while. When he recovered, he thought that the time was one week later than in fact. In this instance he lost antecedent memory, never recovering it. There was an excision of memory but no confusion. Other cases are cited. Antecedent memory may not be lost, but there is always an excision. One of Somerville's experiences was used by the Lord Advocate in the famous Merrett trial: A young bicyclist, after a collision with another bicyclist, awoke, after the resulting unconsciousness, to find a doctor waiting on him. He concluded that the doctor had run into him, as he had no recollection of seeing the other bicycle. Somerville cites the following points gained from his cases: Actual accurate memory is retained up to some point which may be just before the accidental bump or even a week previous; there is unconsciousness, with excision of a portion of the memory. There is confusion as to subsequent events but not as to those before the accident.

NEFF, Kansas City, Mo.

ACUTE ASEPTIC MENINGITIS. JOHN GIBBENS, Lancet **2**:12 (July 4) 1931.

Acute aseptic meningitis is not a new disease. It has been described under various terms: benign aseptic purulent meningitis (Schiff), acute idiopathic benign serous meningitis (Andersen and Walff), epidemic meningitis serosa (Eckstein) and acute aseptic meningitis (Gunther). It has the following characteristics: (1) an acute onset with definite meningeal signs; (2) meningeal changes in the cerebrospinal fluid; an increase in pressure and in the number of cells, but sterile results on cultures; (3) a uniform clinical symptomatology; (4) a relatively short benign course without secondary complications; (5) no epidemiological connection with any known infectious meningeal disease, and (6) no local infection. The symptoms are headache, vomiting, a stiff neck, pain in the neck and limbs and often severe, intractable insomnia. Positive Kernig and Brudzinski signs are present, and there is dermographism. In infants the fontanel is found to be bulging. Eye signs are frequent, e. g., nystagmus, squint and photophobia. Some authors emphasize the fact that most of the children have sore throat or severe nasopharyngitis. The fever is usually high at the onset. The cerebrospinal fluid is under pressure, and is clear to cloudy. Cells vary from 60 to 1,500 (average from 100 to 250) in number; they are mainly lymphocytes. Protein is increased; Pandy's reaction is positive; the sugar content is normal, and cultures are sterile. Many authors have thought that acute aseptic meningitis is nothing more than a meningeal form of acute poliomyelitis. Three cases are reported.

LANGMANN, New York.

THE CREASES ON THE MINIMAL DIGIT IN MONGOLISM. L. S. PENROSE, Lancet **2**:585 (Sept. 12) 1931.

The little finger has normally a distal single crease nearly opposite the distal interphalangeal joint, a medial double crease just below the proximal interphalangeal joint and a basal digital line which is complex. In the anomaly described here, a new, usually double, crease takes the place of the distal and medial creases, and lies between the distal and proximal interphalangeal joints.

LANGMANN, New York.

A CONTRIBUTION TO THE STUDY OF THE PHENOMENON OF FALSE ESTIMATION OF WEIGHTS IN THE MENTALLY DEFECTIVE. ANDRÉ REY, Arch. de psychol. **87**:285, 1930.

When two objects of equal weight but of different volume are presented to the average person, the smaller appears to be heavier. A very young child or a mentally defective person does not find this to be true. The absence of this normal illusion is known as the sign of Demoor. The author studied the reaction to this test in forty-two retarded children between 7 and 15 years of age, in thirty-one normal children between 7 and 14 years of age, and in nineteen children between 5 and 6 years of age, to determine whether retarded children who present the normal reaction really do so or whether in them the illusion is less marked than in the normal, and whether the same difference exists between younger and older children. He found that when a feebleminded child presented the illusion, the degree of the illusion was much less marked than in the normal child. This was true also of the younger children. The author is not able to offer any suggestion as to the mechanism that produces the illusion, but notes only that its presence indicates a certain degree of intellectual development.

PEARSON, Philadelphia [ARCH. NEUROL.]

A CASE OF BINASAL HEMIANOPIA. C. DEJEAN, Rev. d'oto-neuro-opht. **9**:28 (Jan.) 1931.

The binasal hemianopias occurring in the course of optic atrophy are accidental and are therefore not discussed. Binasal hemianopia must be caused by bilateral compression of the chiasm, since the direct fibers are mostly in the lateral parts. In chiasmatic lesions there is not a sharp division into two hemifields, one clear and one clouded. Such a picture is due to a lesion of the cortex or the optic tract. In the chiasm all the fibers, direct and crossed, are grouped in a small space. Here the lesion attacks the direct fibers and then encroaches more or less on the crossed bundles.

A boy, aged 7 years, was seen in February, 1929, with a history of visual trouble since the age of 5. He was obliged to hold an object to one side to see it, and in walking he fell over obstacles in his path. His general health was excellent, except for frequent headaches. At 1 year of age, he suffered from nervous crises (loss of consciousness for from one to five minutes, clamped jaws, purple lips and pale facies); there was no jerking of the limbs, foam on the lips, biting of the tongue or loss of urine. These crises occurred at intervals of one or two weeks over a period of two years. Examination of the fields showed a binasal hemianopia reaching and passing the fixation point. The symmetry of the fields in the two eyes was striking. The media and eyegrounds were normal. The vision for colors was somewhat diminished. The Bordet-Wassermann test of the blood gave negative results. Neurologic and general physical examinations revealed nothing abnormal. A roentgenogram of the skull showed a slight enlargement of the sella turcica.

Binasal hemianopias are rare. Cases due to atheroma of the circle of Willis, meningitic exudate, tabes and tumors of the pituitary body have been reported. Rakowicz says that bilateral compression of the chiasm by a tumor cannot occur,

and that binasal hemianopia must be due to a lesion of the eye itself or to a beginning optic atrophy. This may be true of the hemianopias in tabes, but in the case reported there was no nervous symptom or ocular lesion. The headaches and the slight deformity of the sella turcica indicated a chiasmatic lesion. The cause was probably pressure from enlargement of the anterior clinoid process by meningitic fibrosis or by a local osteoperiostitis.

DENNIS, Colorado Springs, Colo. [ARCH. NEUROL.]

THE RECOGNITION OF ASEPTIC PURIFORM MENINGITIS. M. PREBIL, Pediatria **39**:697 (July 1) 1931.

The author presents a review of the literature as to the frequency of aseptic puriform meningitis and adds a detailed account of two such cases coming under his observation. In both of the cases he obtained clinical cures.

SIGNORELLI, New Orleans.

NEUROSES OF THE DIGESTIVE ORGANS. T. GUGLIELMINI, Prat. pediat. **9**:103 (March) 1931.

Neuroses of the digestive tract occurring in infants and young children are described briefly and didactically according to the following classification: (1) nervous anorexia, (2) esophagospasm, (3) cardiospasm, (4) rumination, (5) periodic or cyclic vomiting, (6) nervous gastralgia, (7) pylorospasm, (8) nervous enterospasm, (9) mucomembranous enterocolitis and (10) anospasm. Enterospasmodic conditions are associated with a family history of neurosis, with stigmas of hysteria or with visceroptosis. In these patients, the spread of the arms is greater than the height, the xiphopubic line is greater than the sternal length and the xipho-umbilical line is longer than the umbilicopubic line.

DOOLEY, Kent, Conn.

INVESTIGATION OF THE ANTICONVULSIVE POWER OF CALCIUM ALONE OR ASSOCIATED WITH PARATHYROID OR IRRADIATED ERGOSTEROL IN EPILEPTIC PERSONS. F. DI RENZO, Rassegna di studi psichiat. **19**:1029 (Nov.-Dec.) 1930.

The first attempts to use calcium in the treatment for epilepsy were due to Sabbatani, and were followed by the work of others who found a diminution of calcium in the blood of epileptic persons (Parhon, Longo, Barlocco and others). Alkalosis emphasizes the diminution of calcium in the blood. Pagniez, Wollmer and Bigwood believed that convulsive seizures are due to the diminution of the iron calcium in the blood as a result of alkalosis. In contrast to the favorable results of the action of calcium on epileptic persons are the reports of Klein and Forcione, who have even found a tendency toward an increase of attacks.

Di Renzo has used various calcium compounds intravenously, or intramuscularly. He used a parathyroid preparation and as vitamin D, an irradiated ergosterol preparation. Vitamin D and parathyroid substance were given in order to favor the metabolism of calcium and its exchange between blood and tissue so as to produce hypercalcemia. Seventeen cases were studied, and treatment was given for an average of two months. As a result of the investigation the author concludes that epileptic seizures are not favorably influenced by the use of calcium preparations even when the calcium is in the best condition to be assimilated. The conception, therefore, that epileptic seizures are due to hypocalcemia must be discarded.

FERRARO, New York.

JUVENILE DEMENTIA PARALYTICA. P. CUBINA and A. M. ABRIL, Rev. Psiquiat. & Neurol. (Habana) **2**:103 (March) 1931.

The authors' case was that of a boy of 11 years. The family history was irrelevant. The symptoms were those of generalized progressive muscular weakness. The Wassermann reaction was four plus, as were the Pandy and Ross-Jones tests. The Lange curve was paralytic. The treatment instituted consisted of arsenicals alternating with bismuth and quinine.

SANFORD, Chicago.

A CASE OF MICROCEPHALY WITH SPASMOPHILIA INFERIOR. CARLOS ESCABOR BENAVENTE, Med. de los niños **32**:49 (Feb.) 1931.

A boy, aged 2 years, weighing 5,400 Gm., at birth, was delivered with forceps after a difficult labor. He suffered a birth injury: facial paralysis of two months' duration and a left hemiplegia. He had convulsions several times during the first two years. At the age of 2 years he was mentally deficient but had cerebral spastic paraplegia. Other types of mental deficiencies, amaurotic family idiocy and mongolism are discussed with especial reference to the differential diagnosis.

DWYER, Kansas City, Mo.

A METHOD OF DETERMINING THE DISTANCE FROM THE SKIN TO THE DURA MATER IN CISTERNAL PUNCTURE. MARIANO R. CASTEX and LUIS E. ONTANEDA, Prensa méd. argent. **17**:583 (Sept. 20) 1930.

The distance which separates the skin from the dura mater in the cervical region varies in different persons. It is useful to know this distance in doing cisternal punctures. The authors describe and discuss the various methods devised in the past for measuring this distance, as well as one of their own. By measuring over a hundred skulls it was found that the posterior margin of the foramen magnum bore a definite relationship to the line bisecting the tips of the mastoid processes. In about 40 per cent the distance from the posterior lip of the foramen magnum to the intermastoid line measured 25 mm. The remainder of the measurements varied only a few millimeters on either side. In the application of this method, by means of an ordinary carpenter's square the distance from the back of the neck to the tip of either mastoid process is determined. Twenty-five millimeters are subtracted from the measurement, the remainder indicating the distance from the skin to the dura.

HARRISON, Iowa City.

THE EFFECT OF CISTERN PUNCTURE ON THE BLOOD NITROGEN AND BLOOD CHLORIDES. MARIO SCHTEINGART, LUIS E. ONTANEDA and JOSE F. RINALDI, Rev. Soc. Argent. de biol. **6**:555 (Nov.) 1930.

Estimation of the blood urea, residual nitrogen, incoagulable nitrogen and chlorides was made in a total of fourteen patients suffering from a variety of diseases, including syphilis, acromegaly, hepatic cirrhosis and malignant hypertension. The blood nitrogen underwent variable modifications in different subjects. The most notable variations were in two cases of malignant hypertension; in one the blood urea and the incoagulable nitrogen rose to 0.27 and 0.20 per cent respectively; in the other case there was a gradual fall to 0.38 per cent at the end of six hours. Blood chlorides were elevated in 87.5 per cent of the patients examined. These variations were considered to be independent of modifications of the blood volume. The authors feel that the changes are brought about by the mechanical action of the extraction of the spinal fluid, which alters the subarachnoid tension.

HARRISON, Iowa City.

PATHOLOGIC ANATOMY OF THE PALLIDAL FORM OF ATHETOSIS. M. M. AMMOSOW, J. f. Psychol. u. Neurol. **41**:374, 1931.

A boy, aged 6, who was born prematurely in the seventh month of pregnancy, began to show, at the age of 2 months, a progressive muscular rigidity

associated with choreo-athetosis. The abnormal movements were predominantly athetosic. There was no history of infection, trauma to the head, difficult labor or asphyxia. A hereditary factor was suspected, but could not be definitely ascertained. The disease was undoubtedly extrapyramidal, with some features of Wilson's disease, such as dysarthria and partial dysphagia. Histologic examination revealed definite evidences of a system disease in which the nerve fibers primarily and the nerve cells to a lesser extent presented a retrograde degeneration. The pallidum showed deposits that were well brought out by intensive staining with hematoxylin; these also gave indefinite reactions for iron and calcium. The myelin sheaths showed a peculiar scaly formation, which is regarded by Ammosow as the end-product of myelin disintegration. The disease is considered by Ammosow as due to a congenital "weakness" of the extrapyramidal nerve fiber system. In this respect it differs from the striatal form of athetosis, in which the status marmoratus is the result of a primary destruction of nerve parenchyma, which is associated with a proliferation of glial tissue and of myelin fibers. Clinically, these two forms of athetosis are distinguished from each other by the fact that the striatal form is preeminently stationary or regressive, while the pallidal form is progressive. It may be, however, that clinico-anatomically the character of the pathologic changes is not of as much significance as the localization of the process (pallidum), so that one is perhaps justified in thinking of a form of pallidal athetosis that differs genetically as well as anatomically.

KESCHNER, New York.

FURTHER STUDIES ON THE TETANIC ACTION OF THE URINE EXTRACT OF SPASMOPHILIC BABIES. A. NITSCHKE, Ztschr. f. Kinderh. **50**:662 (March) 1931.

In twelve additional cases, as well as a total of twenty-two, a substance was found in the urine, the injection of which into rabbits caused the syndrome described by Nitschke, lowering of calcium in the serum, electrical hyperirritability, convulsions and death. The urine extract of control children, previously spasmophilic, studied after cure, showed no such substance and no clinical symptoms in the rabbits. The theory presented before, that spasmophilia in babies depends on an excessive function of the lymphatic system, is supported by the larger number of cases.

EMERSON, Boston.

PATHOLOGIC DEVIATIONS OF INSTINCT IN CHILDHOOD. J. K. FRIEDJUNG, Ztschr. f. Kinderh. **50**:781 (March) 1931.

Friedjung describes three cases of pathologic deviations of the sex instinct: (1) a boy, 16 months old, who went into a tantrum if he could not have his mother's stocking to sleep with; (2) a boy, 8 years old, who, after having had a painful wound on the thigh, found pleasure in beating himself with a stick; (3) a girl who had palpitation of the heart and anxiety, one and one-half years after an attack of diphtheria. All three lived in the same room with the parents.

EMERSON, Boston.

RECTAL INJECTION OF ETHER IN THE TREATMENT FOR CHOREA MINOR. K. KONISHI, J. Pediat. (Tokyo), May 20, 1931, no. 372, p. 712.

The author reports the results of ether injection in the treatment for chorea minor at the Osaka district meeting of the Japan Pediatric Society. The dose recommended is from 15 to 20 cc. of 5 per cent ether in oil, given as a retention enema three times daily after thorough irrigation of the colon. The effect is usually seen in from five to twenty days after the commencement of treatment. The author saw a definite result in four patients ranging in age from 7 to 12 years.

KATO, Chicago.

Diseases of the Eye

CONGENITAL TOTAL COLOR BLINDNESS. W. E. FRY, Am. J. Ophth. **13**:1064 (Dec.) 1930.

The author discusses the explanation of congenital total color blindness according to the different theories of color vision. The case reported is the eighth in this country. A woman, aged 23, came under observation because of day blindness. Vision was so poor on a bright day as to prevent her getting about, though she could do so very well in dim light. She was totally color blind. Corrected vision was 6/60 in the right eye and 6/30 in the left. The eyes were normal externally, though a short lateral nystagmoid movement could be detected on ophthalmoscopic examination. The fundi and the fields were normal.

REESE, Philadelphia [ARCH. OPHTH.].

EARLY TREATMENT OF THE CROSS-EYED CHILD. E. K. HALLOCKS, New York State J. Med. **31**:745 (June 15) 1931.

The author outlines the causes and treatment of strabismus. He urges that the condition be corrected early in life.

AIKMAN, Rochester, N. Y.

A TRACHOMATOUS FATHER CONTAMINATES HIS THREE CHILDREN THROUGH THE AGENCY OF A MORAX DIPLOBACILLUS CONJUNCTIVITIS. J. SEDAN, Rev. internat. du trachome **8**:62 (April) 1931.

The mother of three children had been treated for trachoma since 1927. As is the custom, the children were examined at the incipiency of the mother's condition, and at various periods following. The mother was advised as to the contagiousness and kept a rigid toilet, so that there were no signs of the children being contaminated. The father was away from the family until January, 1930. On his return to them, and also to the clinic, he, too, was advised of the seriousness of the trachoma that affected him. In May, the father presented himself at the clinic with a diplobacillus conjunctivitis. This infection lasted about three weeks. In July, the three children were examined, and all showed a beginning trachoma. At the same time the father had a fresh exacerbation of trachoma. The author calls attention to a similar case which he reported to the League Against Trachoma, in January, 1926. He agrees with the late William Nicati, who was wont to repeat that "trachoma in the secreting stage is dangerous to all and more apt to be disseminated."

MAYER, Chicago [ARCH. OPHTH.].

THE ETIOLOGIC RELATIONSHIP BETWEEN TRAUMA AND SARCOMA OF THE ORBIT. A. TRETTENERO, Ann. di ottal. e clin. ocul. **59**:272 (March) 1931.

The author's patient was a child of 3 years who, in a fall, had wounded the right eye and orbit on a sharp object. Traumatic cataract developed, which was removed a month after the accident, with apparently a good result. Two months after the operation, vision had decreased, the tension was raised and right exophthalmos was present. A detachment of the retina was seen which did not transilluminate clearly; therefore, enucleation of the eye alone was performed. Sections showed an intra-ocular tumor which was considered by the author, after study of sections, to be a mixed cell sarcoma. Two months later a new growth was present in the orbit. Evisceration of the orbit was refused, and the child died three months later.

The reported cases of orbital sarcoma following trauma are reviewed. In most cases doubt existed as to the etiologic importance of the trauma. In the author's case the possibility of an etiologic relationship could not be excluded. It is definitely known that trauma may accelerate and aggravate the course of a new growth already present.

GIFFORD, Chicago [ARCH. OPHTH.].

WHAT REGULATIONS ARE EMPLOYED IN PROGRESSIVE JUVENILE MYOPIA? J. MELLER, Wien. klin. Wchnschr. **44**:21 (Jan. 2) 1931.

A discussion of the proper glasses includes about three fourths of this article. Reference is made to the theory of Javal that convex lenses are indicated, as the accommodation is strengthened by such lenses. The mere fact that concave glasses increase distance vision should be sufficient to satisfy the need for them. Overcorrection with the concave lens is common, but is usually due to incompetence or to mass examinations. No brief is held for the hypothesis that the proper concave lens limits or improves the myopia. There is no truth in the theory that the use of concave lenses will cause decreased visual acuity without glasses. This is simply contrast. The practice of using atropine to paralyze accommodation over a long period of time has no justification. It does limit and blur close work, which is only apparently improved when the administration of atropine is discontinued, but it does not actually retard the progress of the myopia. The method that attempts to influence distance vision by long practice in viewing test types is a physical impossibility, and no amount of psychic influence is able to change such a condition. Whether the use of proper concave glasses retards the progression is not the question, and this is not a contention. The important fact is that in youth all functions are more amenable to correction, and there is no necessity to allow procrastination until the retinal function is no longer tractable, and changes in external muscles and those of accommodation have taken place. Proper glasses make for correct posture of the head and the entire body. All near work that can be eliminated should be, until a time when myopia is stationary. Myopia does not cause tiredness, as witness the fact that myopic students are usually the more diligent ones. The fact that the near-sighted child sees poorly increases his love for near work, because he finds it more satisfactory than trying to play with his better-sighted friends. It is a common occurrence to find children of near-sighted parents less myopic than either parent, owing to proper care. Meller believes that the type with posterior staphyloma is not amenable to any treatment. The hope that removal of the lens in these cases would be of value has not been fulfilled.

MAYER, Chicago [ARCH. OPHTH.].

ANGIOMATOSIS RETINAE (HIPPEL'S DISEASE). G. F. ROCHAT, Nederl. tijdschr. v. geneesk. **75**:437 (Jan. 24) 1931.

In Hippel's disease peculiar rose-colored tumors are observed in the peripheral parts of the retina. These tumors consist principally of an accumulation of hypertrophic capillaries, which has given rise to the name angiomatosis retinae. The disease has a progressive course and often gives rise to cerebral tumors. It often has a familial character. Several families are known in which different members one after the other died from this disease at an early age. The author gives his experience in one family with this disease which had been controlled for eleven years. Heredity was clearly demonstrated for three generations. The development of the retinal tumors could be studied in the many preparations obtained in this family and compared with the clinical picture. In the three cases that came to autopsy the cerebral tumors were principally situated in the cerebellum, but tumors could also be found in other parts of the nervous system.

VAN CREVELD, Amsterdam, Holland.

TWO CASES OF CURED SYMPATHETIC OPHTHALMIA. E. PUSCARIU, Cluj. med. **11**:416, 1930.

A boy, 15 years old, suffered from a perforating injury of his left eye with prolapse of the iris. Therapeutic excision of the prolapsed portion of the iris, thermocautery and conjunctival autoplasties were employed. After six weeks there appeared a bilateral sympathetic iridocyclitis, which was treated by atropine,

injections of milk, intravenous injections of methenamine, arsphenamine and mercury. After two months he was symptom-free. Vision was: right eye, 1; left eye, 1/6.

A boy, 7 years old, suffered from a severe perforating injury to the left eye. After fifty days there presented a sympathetic ophthalmia of the right eye with uveitis, deposits on Descemet's membrane, synechiae of the iris and a hypotonic painful eyeball. Cure with clearing up of the inflammatory phenomena was secured. The acuteness of vision, however, remained reduced.

BLATT, Tagu-Mures, Roumania [ARCH. OPHTH.].

MULTIPLE AND BILATERAL CONGENITAL MALDEVELOPMENTS IN A PATIENT WITH SPECIFIC CHORIORETINITIS. NICOLAU-CLIMESCU, Cluj. med. **11**:420, 1930.

A man, 47 years of age, had undergone a marked impairment of vision in a few months. He had bilateral choroiditis with vision as follows: right eye, finger counting at 1 meter; left eye, finger counting at 2 meters. He presented a series of malformations as follows: slight protrusion of the disks and irregularity of their borders, dimples on the disk and an epipapillary membrane in the right eye. After two years, vision was: right eye, finger counting at 2 meters; left eye, finger counting at 4.5 meters. In the right eye, the visual field for white and colors was markedly contracted.

The authors are of the opinion that the functional troubles were due to the specific chorioretinitic process, but not to the congenital malformations.

BLATT, Tagu-Mures, Roumania [ARCH. OPHTH.].

Diseases of the Ear, Nose and Throat

THE IMPORTANCE OF DIAGNOSING AND TREATING SINUSITIS IN INFANTS AND CHILDREN. B. C. MARANTZ, Arch. Pediat. **48**:365 (June) 1931.

The author feels that infants are "just as frequently victims" of sinusitis as are older children. He deplores the lack of emphasis given to this phase of sinusitis, and is astonished that most texts ignore it or, at the most, give it bare mention. The article contains a description of the anatomy of the sinuses and discusses the diagnosis from the standpoint of symptoms and signs. Complications and sequelae of sinus infection as it occurs in infants and children are discussed, as is the treatment.

WADDELL, University, Va.

THE DEAF CHILD. RICHARD L. BOWER, Wisconsin M. J. **30**:5 (Jan.) 1931.

Over 30 per cent of inmates in institutions for deafness are children with the type which might have been prevented. This acquired deafness commonly follows acute febrile conditions, particularly infections of the nose and throat, measles, scarlet fever and meningitis, during the first five years of life.

Congenital deafness is of biologic origin, with developmental defects largely inherited or of pathologic source, usually syphilitic or tuberculous, present at birth. In the otosclerotic variety, deafness occurs at about the age of puberty. Marriage of the congenitally deaf is to be avoided, as is consanguineous marriage even though free from defect.

Functional testing for hearing before the sixth year of life is only partially satisfactory. The auropalpebral reflex of Bechterew obtained with the aid of a C4 fork is best. The deaf child does not laugh. It is a mistake to consign a partially deaf child to a school for the deaf. During acute infections, a child's ears should be closely watched and the drums opened at the first sign of infection of the middle ear. Early removal of the tonsils and adenoids should be done when ear trouble begins.

JANNEY, Milwaukee.

Surgery and Orthopedics

EPIPHYSITIS OF ADOLESCENTS, WITH SPECIAL REFERENCE TO ETIOLOGY. LESTER A. SMITH, Am. J. Roentgenol. **22**:127 (Aug.) 1929.

The epiphyseal lesions usually included are adolescent coxa vara, or slipped epiphysis, a juxta-epiphyseal lesion and osteochondritis of the vertebral body. Other authors also include osteochondritis dissecans, syphilitic osteochondritis or epiphysitis, rickets, both early and late, typical endocrine epiphyseal changes, scurvy and typical infectious lesions. Almost any bone may be involved, but rarely is there involvement of the bones not subject to direct or indirect trauma, muscular strain or static stress. The etiology is: (1) trauma, (2) alterations of the blood supply, (3) infection, (4) abnormalities of bony development, (5) constitutional conditions affecting bone and (6) disturbances of innervation. The pathologic sequence is interruption of epiphyseal nutrition, necrosis, pathologic fracture, viability of articular cartilage and replacement of necrotic bone. The case reports include several cases of silent epiphyseal lesions, which are probably more common than has been the belief. Lesions of various epiphyses associated with infection tend to indicate that infection is a probable cause of many of the lesions.

STULIK, Chicago.

UNDESCENDED TESTIS: PRINCIPLES AND METHOD OF TREATMENT. HUGH CABOT and REED M. NESBIT, Arch. Surg. **22**:850 (May) 1931.

Reviewing the literature on undescended testis, the authors conclude that orchidopexy had probably best be performed before the age of 9; that even after puberty and including the third decade the operation may save a gland capable of some spermatogenesis, and that on account of active interstitial cell development in the glands, orchidectomy should never be given consideration at any age. Various forms of orchidopexy are described, and twenty-five cases are reported with recent data in which a new technic was applied, the principle of which was to obtain a permanent lengthening of the vessels by continuous stretching. The late results were good, showing that the procedure is safe, simple and apparently physiologic.

KAISER, Rochester, N. Y.

POSTOPERATIVE PULMONARY ATELECTASIS: OBSERVATIONS ON THE IMPORTANCE OF DIFFERENT TYPES OF BRONCHIAL SECRETION AND ANESTHESIA. A. LINCOLN BROWN, Arch. Surg. **22**:976 (June) 1931.

Experimentally in animals the author demonstrated that the introduction intratracheally of sputum impregnated with iodized poppy seed oil produced postoperative lobular atelectasis. When thick viscid sputum was injected, it did not penetrate deeply and was arrested at the orifices of the larger bronchi, while thin sputum penetrated deeply and filled the bronchi. The author observed the course of postoperative pulmonary complications following practically all types of anesthetics. His impression is definite that the incidence of pulmonary atelectasis is greater following spinal anesthesia than following any form of inhalation or regional anesthetic. Spinal anesthesia encourages thick, tenacious sputum to plug the larger bronchi. The experimental and clinical observations are compared and are found to agree.

KAISER, Rochester, N. Y.

PERITONITIS: AN EXPERIMENTAL STUDY OF HEALING IN THE PERITONEUM AND THE THERAPEUTIC EFFECT OF AMNIOTIC FLUID CONCENTRATE. HAROLD M. TRUSLER, Arch. Surg. **22**:983 (June) 1931.

In order to facilitate the postoperative course in abdominal surgery and reduce the incidence of adhesions, experimental studies were made to watch the effect of amniotic fluid concentrate on the postoperative healing. The experimental

studies indicate that amniotic fluid concentrate, when injected into the traumatized peritoneum, produces a reaction stimulating the normal processes of repair and thus minimizing postoperative adhesions. In the presence of contamination, this reaction likewise inhibits the development of fatal peritonitis, but there is no evidence that it can exert a beneficial action when a far advanced peritonitis is encountered at operation.

KAISER, Rochester, N. Y.

INFECTIONS OF THE ORAL CAVITY. H. S. DANNING, Bull. New York Acad. Med. **7**:14 (Jan.) 1931.

The mouth is a very unclean cavity, and bones of the jaws become infected more often than any other bones of the body. The mandible and maxillary bones become infected through the gum attachment, the gingival and peridental route, or through caries in the teeth opening into the pulp and by way of the canal into the bone. There is also the hematogenous route. In children, bone infections spread rapidly through the follicles of the erupting teeth with serious destruction of tissue. The infection also retards development of the jaw bone, predisposing to unsightly facial deformities. Early treatment is patently a most important factor. A pulpless tooth is a menace in the mouth. Every infected tooth in a childd should be extracted long before it has had a chance to involve the bone. Bone abscesses in the face should be incised immediately after the diagnosis is made.

Gingivitis of the catarrhal type is usually of bacterial origin (*Micrococcus catarrhalis* and the pneumococcus). Traumatic gingivitis is frequently met with and is often caused by the tooth brush. Most of the tooth brushes are unclean, and many of them are too stiff, causing abrasion of gum margins.

Necrotic gingivitis in childhood is usually a complication of the acute infectious diseases associated with marked systemic reactions, foul breath and glandular involvement. It may start around one tooth and spread to the others. The ulceration may heal in one place and break down in another. Unless strict mouth hygiene (mild antiseptic washes) is adhered to, the condition tends to recur weeks or months following an apparent cure.

JAHR, Omaha.

INDICATIONS FOR UROLOGICAL EXAMINATIONS IN INFANTS AND CHILDREN. MEREDITH F. CAMPBELL, M. J. & Rec. **197**:392 (April 15) 1931.

The indications for urologic examinations are the same in infants as in adults. This, unfortunately, is not generally appreciated. In the author's opinion the commonest reasons for a complete examination are pyuria, disturbances of micturition, hematuria, tumors and pain. If pyuria does not clear up after fourteen days of medical treatment, a urologic examination should be made. If a suprapubic mass is palpable, or if hematuria not due to hemorrhage nephritis is present, an examination should be made. The author found it more difficult to convince the attendinng physician of the advisability of the examination than to convince the parents of the child. Children stand the cystoscopic examination far more easily than do adults. In view of the minimal risk entailed, one should adopt a more liberal attitude toward these investigations than has customarily been exhibited in the past.

WILLIAMSON, New Orleans.

A VAGINAL SPECULUM FOR USE IN CHILDREN. HERSCHEL HEINZ, New England J. Med. **204**:607 (March 19) 1931.

In vaginal disease of childhood the corrective diagnosis and treatment depends primarily on the thorough inspection of the involved areas. This can be accomplished by a simple improvised nasal speculum. The blades are lengthened and a set screw attached to hold the blades open. Illumination is furnished by a stand lamp and head mirror. The lubricated blades are inserted with the handle horizontal, at right angles to the long axis of the vulva.

GENGENBACH, Denver.

THE TREATMENT OF APPENDICITIS IN CHILDREN. G. MASSABUAU, Progrès méd., June 6, 1931, p. 1033.

The author divides appendicitis in infants and children into two groups. The first group consists of those seen in the first thirty-six hours. These patients should all be operated on, and the prognosis is excellent. The second group are those seen later. Treatment depends on the symptoms. It is not desirable to operate unless the condition is rapidly becoming bad. Usually time can be taken to allow a better state of health to develop.

SANFORD, Chicago.

THE SYNDROME OF PALLOR AND PYREXIA FOLLOWING OPERATIONS IN CHILDHOOD. G. MASSABUAU, Progrès méd., June 27, 1931, p. 1180.

The author calls attention to the syndrome of pallor and highly rising temperature frequently seen from four to five hours postoperatively in children. This is distinguished from hemorrhage by the fever, from bronchopneumonia by the lack of cyanosis and from septicemia by the time element and lack of local symptoms about the operative wound. The cause is not definitely known, although intoxication, anaphylaxis and nervous shock have been thought causative. The prophylaxis is general ether anesthesia, forcing of fluids after operation and administration of epinephrine and digitalis to combat hypotension.

SANFORD, Chicago.

TREATMENT FOR CONGENITAL DISLOCATION OF THE HIP. CHARIER, Rev. d'orthop. **18**:118 (March) 1931.

Charier discusses the various methods of treatment for congenital dislocation of the hip. His choice is the ordinary method using three positions: (1) tibia horizontal; external rotation of 90 degrees; abduction of the thigh 90 degrees; thigh 15 degrees above the horizontal; (2) abduction 45 degrees; flexion 15 degrees; (3) abduction 25 degrees; flexion from 15 to 20 degrees; internal rotation from 50 to 60 degrees. The positions are illustrated. To avoid stiffness in the joints, Charier uses what he terms a "plaster with a free space." By the use of this apparatus slight motion in a definite direction is permitted, thus overcoming liability to stiffness in the joint. In the construction of this apparatus, excessive padding is placed about the thigh in the direction in which motion is to be permitted. The plaster surrounding the knee is cut away and the excessive padding removed, leaving a space between the thigh and the plaster. Since flexion-abduction is the only safe motion to permit, the excessive padding is applied to the anterior surface of the thigh.

RYAN, Vancouver, B. C.

OSTEITIS OF THE RIBS WITH SPONTANEOUS FRACTURE. ÉTIENNE SORREL and PAUL BUFNOIR, Rev. d'orthop. **18**:232 (May) 1931.

Osteitis of the ribs is common, but spontaneous fracture in osteitis is much rarer than is commonly believed. A child, 4 years of age, was brought to the hospital with a swelling on the right side of the thorax at the level of the fourth and fifth ribs. The tuberculin skin reaction was markedly positive, the Wassermann reaction negative and the general health poor. A question arose as to whether there was a burrowing abscess from dorsal Pott's disease or a localized infection. Roentgenograms of the ribs at this age give little information of value. Iodized poppy seed oil 40 per cent was injected into the abscess, and showed it to be localized. Aspiration did not cause healing. On exploration, there was an absence of the fifth rib for about 3 cm., the posterior end being covered by periosteum. The sternal end was jagged and scooped out for a distance of 2 cm. (up to the cartilaginous junction). The pleura was healthy, as it usually is in such cases. After clearing away diseased tissues, the wound was closed and healing occurred by primary union. In the treatment for such condi-

tions, simple aspiration should be tried first. If that fails, the abscess cavity should be opened and cleaned out, the abscess walls dissected out and the wound closed. Healing is usually prompt.

RYAN, Vancouver, B. C.

EMPYEMA. MARTINEZ VARGUS, Med. de los niños **32**:65 (March) 1931.

A girl aged 16 months was found to have empyema four months after bronchopneumonia. Rib resection and irrigation with surgical solution of chlorinated soda effected a prompt recovery. The second patient was a boy aged 4 years. Empyema of the left side occurred two months after bronchopneumonia. A friction rub was heard over the area of greatest dulness, with complete absence of breath sounds. This unusual sign was caused by the formation of fibrinous adhesions in the pus. The exudate broke through the pleura and was drained by resection of part of the seventh rib in the midaxillary line. The pneumococcus was isolated. The child was completely well in one month. The third patient was a girl of 7 years. Three months after pneumonia, she presented the typical signs of empyema of the left side of the chest on a level with the left nipple in the axillary line. A tumor about the size of an egg appeared with redness, heat and fluctuation. The day following, it suddenly became larger and filled with pus (empyema necessitatis). Operation was refused and the child died of septicemia.

DWYER, Kansas City, Mo.

REPORT OF CASES. V. WALTER, Arch. f. klin. Chir. (Congressbericht) **162**:61 (Nov.) 1930.

The author presented many cases of congenital malformations of the spinal column. He demonstrated a case of a supernumerary vertebra. The supernumerary vertebra took on a wedge shape due to pressure from the adjacent vertebrae. These cases are not usually recognized early in childhood. They are diagnosed by the roentgenogram. The author also demonstrated a case of anterior and posterior spina bifida, a congenital elevation of the scapula and incomplete fusion of the ribs with their transverse processes.

KOHN, Milwaukee.

REPORT OF CASES. HEILE, Arch. f. klin. Chir. (Congressbericht) **162**:83 (Nov.) 1930.

The author showed that in 90 per cent of the obstructions of the pylorus in which tumors can be felt, a typical roentgenogram can be demonstrated, that is, a complete closure of the pylorus for three hours or longer, a dilatation of the stomach, increased stomach secretion and peristalsis, and dextroposition of the pylorus. These cases are relieved by the Rammstedt operation, after which the stomach empties itself rapidly. The remaining ten per cent do not show this rapid evacuation even after the operation. This is because these are primarily spasms and are not entirely affected by operation. The severity of these cases from a roentgen standpoint is not borne out by the clinical picture. The patients usually recover.

KOHN, Milwaukee.

Miscellaneous

THE THERAPEUTICS OF ULTRAVIOLET LIGHT. ALFRED F. HESS, Bull. New York Acad. Med. **7**:282 (April) 1931.

Sunlight has always been recognized as a beneficial agent in the treatment of disease, but it took experimental work to show definitely and specificially that the invisible ultraviolet rays have curative properties for rickets. The present status of ultraviolet activity is overemphasized by the laity due to high pressure propaganda.

The actual therapeutic properties of ultraviolet rays are limited. In reality, their only curative effect may be demonstrated in rickets. They are of some value in the treatment for tuberculosis of the skin, bones, joints and glands, but are of no benefit in pulmonary tuberculosis. They are also of some value in some skin disorders, notably in such ordinary infections as furunculosis. There is no evidence that ultraviolet rays have any beneficial effect in the prevention of colds or in the treatment of nervous disorders. There is no basis for suspecting that these invisible rays can instill new energy in tired persons. Overirradiation may produce severe burns or an overstimulation of the nervous system with subsequent depression. Ultraviolet lamps have no place in beauty parlors or athletic clubs, and ultraviolet exposure should be under supervision of the physician and not be left to the caprice of the individual. Windowpanes which allow the passage of a considerable percentage of ultraviolet rays are of value in sanatoriums or in children's rooms where there is much access to sunlight, especially where there is a southern exposure. To furnish this kind of window glass to office buildings where the light is obstructed by adjacent structures serves no purpose whatsoever, for the ultraviolet rays are of value only if they impinge directly on the surface of the body.

JAHR, Omaha.

STRYCHNINE POISONING. JOHN AIKMAN, New York State J. Med. **31**:219 (Feb. 15) 1931.

Study of this subject shows that strychnine poisoning is the most common fatal poisoning in small children. It is due to the careless habit of leaving attractive and pleasant tasting tablets about the home. Most of these tablets are cathartics like A. B. & S., A. B. S. & C. and Hinckle's; or tonic tablets containing strychnine or nux vomica. The laws in New York that control the sale of such tablets and even tablets containing strychnine alone are very lax. The following suggestions are made for the reduction of these deaths: (1) Education of the public. (2) Poison labels or special labels as to danger for children. (3) Restriction of sale of strychnine except on prescription. (4) Elimination of the colored sugar coating on the tablets. If tablets containing strychnine or nux vomica were never so coated, fewer cases of poisoning would result. The bitter taste would prevent the ingestion of a dangerous amount of the drug.

AUTHOR'S SUMMARY.

AN APPRAISAL OF PRESENT DAY METHODS OF RAISING CHILDREN. FRANK VAN DER BOGERT, New York State J. Med. **31**:343 (March 15) 1931.

Medical education of the public may be productive of harm. A distinction should be made between hygiene and medicine. Too much attention directed to the removal of tonsils and to vitamins, height and weight tables and psychoanalysis react unfavorably on the child. The author asks for more rational care of children.

AIKMAN, Rochester, N. Y.

MOTTLED ENAMEL IN A SEGREGATED POPULATION. G. A. KEMPF and F. S. MCKAY, Pub. Health Rep. **45**:2923 (Nov. 28) 1930.

This communication deals with a statistical report on the occurrence of "mottled enamel" in the teeth of the residents of Bauxite, Ark., a mining town using deep well water and a few springs as its sources of water supply. The study was undertaken to ascertain whether a relationship existed between the water supply and the high incidence of "mottled enamel" prevalent there, and is based on the examination of over 450 school children ranging in age from 5 to 18 years, so as to include observations on the temporary, as well as on the permanent, teeth. "Mottled enamel," also known as "denti di Chiaie" after Stefano Chiaie of Italy, was first described in this country by Eager who pointed out its intimate connection with certain types of water supply. Investigations carried

out subsequently by Black and by McKay showed the presence here of many endemic centers particularly in mountainous regions where deep well water is used, the supply being replenished by water trickling down from the mountains. It is a condition affecting the permanent teeth, mostly the labial surfaces of the upper incisors and cuspids. It is characterized grossly by the ghastly opaque white mottling of the enamel which may be stained yellow or brown or even black, the pigment imparting the color being called "brownin," which is said to be manganese. Microscopically there is an absence of cementing substance between the enamel rods in the outer portions of the enamel layer. It is rare to find mottling of the deciduous teeth, a fact which is explained on the basis of the differences in the time of development of the temporary and the permanent teeth.

From the data obtained in the course of their study, Kempf and McKay are of the opinion that there is a specific agent or condition in the village of Bauxite which interferes with the normal development of the enamel of the permanent teeth, an agent strictly limited to the village, not related to food supply or to physical condition and affecting the children of the well-to-do as well as those of the poorer classes. They believe this agent to be the central deep well water supply of the community and give the following reasons for their belief: No case of enamel defect was found which antedated the introduction of the deep well water; that the oldest person found with this enamel defect was born about the time when the deep well water was introduced; that all persons in the community who had used the deep well water during any considerable period of enamel formation exhibited this defect; that no person in the community whose enamel had developed elsewhere exhibited this defect, and that certain persons who, although residents of the community and attending school there, lived beyond the distribution of the deep well water and depended on the original shallow wells exhibited only normal enamel. As a control test, 124 children of the neighboring town of Benton, using river water as its source of supply, were examined. No cases of mottled enamel were found except in 11 of the children who had lived in Bauxite during the period of their enamel formation. Chemical analysis of the water supply of Bauxite has shed no light as to the probable causal agent. A complete bibliography on the subpect is given.

ABRAMSON, New York.

FOREST AND OPEN AIR SCHOOLS. K. TRIEBOLD, Rev. Leag. Red Cross Soc. **12**:89 (March) 1931.

The advantages of open air education are stimulation to the body systems and promotion of quick intelligence. It provides a home for delicate children and promotes a healthy life.

SANFORD, Chicago.

THE SIGNIFICANCE OF THE THYMIC AND THYMICOLYMPHATIC STATUS IN LEGAL MEDICINE. WIKTOR GRZYWO-DABROWSKI, Ann. de méd. lég. **11**: 128, 1931.

Persistent thymus occurs in healthy persons as old as from 25 to 35 years of age. It is not a predisposing factor to sudden death. This statement applies also to the thymicolymphatic state. There is no objective proof that this state, or that a persistent thymus, influences the constitution. The thymus does not persist longer in those committing suicide than in those who die suddenly from other causes.

AUTHOR'S SUMMARY.

THE FOSTER HOME SYSTEM. B. NYBERG, Rev. internat. de l'enf. **11**:242 (March) 1931.

Throughout human history, the practice of adopting orphans and abandoned children has prevailed, while institutional care has been provided only since the Christian era. Each method has its advantages, but a normal child certainly fares better in a home than an asylum. For those requiring special care or individual instruction, institutional life seems more desirable.

A history of these systems is outlined by the author. In Finland there is an organization, founded in 1922, the chief purpose of which is the establishment of receiving stations for abandoned children. From these depots, children are placed in suitable homes, the foster parents being subject to regular inspection. They are paid monthly through the society's bureau. It is reported that 65 per cent of these foster parents are well-to-do farmers, 25 per cent are trained artisans, foremen or teachers and 10 per cent are shopkeepers or government officials.

AMESSE, Denver.

THE CHILD'S PLACE IN AFRICAN RELIGIONS. E. TORDAY, Rev. internat. de l'enf. **11**:331 (April) 1931.

In a paper read before the British Committee of the International Conference on African Children, the author stressed the importance of a sympathetic attitude toward the native religion if sociological and hygienic measures are to succeed. He called attention to the well known fact that fetishism takes the place of religion throughout Africa, and that this pseudoscience, while countenancing many reprehensible doctorines, is probably no worse than the medieval medicine of Europe. The aborigines believe that every man has two souls, one derived from the father, the other from the mother; that when a child is born, the only new thing about it is the body, for its souls are simply shoots of those of its parents. This theory of reincarnation is so firmly implanted that the newly born child is welcomed and honored as a returned ancestor. It is widely, if not generally, believed that the dead are reincarnated in their grandchildren and that this phenomenon may occur during the ancestors' own lifetime. For this reason a particular intimacy exists between grandparent and grandchild, going far beyond the natural love common to mankind. Clearly one must take these relations into account when one advises African parents how to protect their children.

AMESSE, Denver.

THE SITUATION AMONG UNEMPLOYED CHILDREN IN GERMANY. O. REISE, Rev. internat. de l'enf. **11**:354 (April) 1931.

A considerable portion of the unemployed in Germany, numbering about five million workers in March, 1931, are young people. Most of these boys and girls have completed their apprenticeship in the various trades and can find no opening in their particular sphere of labor; the same obtains in the case of students who have just finished school and find themselves prevented by the economic crisis from taking up an apprenticeship.

The problem may be considered from three points of view: social, economic and political, with the menace always present that among these groups of disappointed, disillusioned youths the antisocial attitude will be strengthened and complete demoralization approached. Deplorably inadequate housing conditions exist everywhere, forcing the young to seek entertainment in the city streets. Recruits are thus easily won for all sorts of political demonstrations, while many find temporary relief, at least, by joining the criminal classes. In Berlin, police statistics show that the number of girls living regularly or occasionally by prostitution amounts to 35,000.

AMESSE, Denver.

TECHNIC AND OBSERVATION OF HELIO-MARINE CURES. G. BARRAUD, Rev. internat. de l'enf. **11**:443 (May) 1931.

The serious menace to the health and life of invalid children through the injudicious use of sea air and sea bathing is stressed again by a senior member of the International Society of Hydrology. The frail organism must be adapted gradually to these powerful elements if a maximum of benefit is to be obtained, and this process involves a knowledge of climatology and heliotherapy not possessed by the average family physician.

The extensive seacoast of France permits specialization in the management of cases sent from the interior. Certain children react favorably in the warm, dry climate of the Mediterranean littoral, while others do better in the cooler regions of the northern coast. The latter seem especially suitable for children suffering from glandular tuberculosis. Barraud outlines the routine management of patients sent for seaside cures, and points out the danger of excessive haste in securing acclimation.

AMESSE, Denver.

THE EFFECT OF UNEMPLOYMENT ON THE YOUTH OF AUSTRIA. O. RUDEL-ZEYNEK, Rev. internat. de l'enf. **11**:475 (May) 1931.

In both manual and eductional directions Austria is developing relief measures for the excessive unemployment in that country. Not only are many thousands of laborers without work, but enormous numbers of children, heretofore employed, are now recipients of the government dole. To minimize as far as possible the distress involved in the unparalleled economic situation, organized effort is extended throughout Austria from a central office known as the Bureau of Child Protection and Welfare. A subdivision of this agency interests itself in securing employment for boys and girls in the agricultural districts; another department develops opportunities for proper vocational guidance and professional training in trades, and a third group specializes in preparing girls for domestic service. In March, 1931, the number of young workers receiving allocations amounted to more than 334,000.

AMESSE, Denver.

MEDICAL PERIODICAL EXAMINATIONS COMPULSORY FOR MINORS IN INDUSTRY. JOAO DE BARROS BARRETO, Bol. Inst. internac. am. de protec. a la infancia **4**:621 (April) 1931.

Periodical medical examinations for all people in general are at present one of the chief aims of preventive medicine. The child is especially well taken care of in its first years of life, that is, during its preschool and school age. Preventive medicine has been also extended to adolescents.

Private health organizations, and American insurance companies in particular, are popularizing the practice of the periodical physical examination. It bears special importance for persons suffering from heart disease, rheumatism or tuberculosis, not only for the sake of diagnosis but also to ensure the adoption of preventive measures against the evil, and, in the case of workmen, to enable them to undertake the sort of labor which is best adapted to their psychophysiologic conditions.

The care of workmen's health is of greater importance in the case of minors. That is why labor legislation establishes a minimum age of 16. Of twenty-six factories that were visited in Rio de Janeiro, only three did not employ minors; in the others there were 1,011 minors employed, working in very defective health conditions, especially those in glass and ink factories, foundries and printing presses. The investigation showed that 70 per cent of these minors were illiterate, that their age was not always the one assumed and that their salaries were small.

The statistics supplied by Austrian and German insurance companies show that morbility and mortality rates are twice as high at 15 as at 14 years of age, and that the number of working days lost in one year by the former group of minors through illness, is also twice as large as that lost by other workmen. In the group from 15 to 19 years of age, tuberculosis is twice as frequent as among adolescents who are not employed in industry.

Minors are more liable than adults to contract disease through forced position, toxic gases, deficiency of air, light, etc., and that is why it is indispensable to adopt the periodical examination as a means of efficient protection.

AUTHOR'S SUMMARY.

THE EVOLUTION OF THE MIMIC. L. KWINT, Ztschr. f. Kinderforsch. **38**:143 (March 12) 1931.

The article is an attempt to study the development of the mimetic activities. Only the voluntary mimic was examined. Twenty-six different kinds of movements were used, and the degree of each muscular movement was studied in a statistical fashion. A test system for children from 4 to 17 years was elaborated. The author discovered that the ability to carry out mimetic movements voluntarily increases with age. Children with decreased mentality show a decrease in their ability to carry out these movements.

REICHLE, Cleveland.

INFLUENCE OF SODIUM THIOSULPHATE ON EXPERIMENTAL LEAD POISONING. N. SUMA, J. Pediat. (Tokyo), April, 1931, no. 371, p. 556.

In view of the fact that sodium thiosulphate was proposed by Ravant, Denni, McBride, Hoffmann, Sasalant, Ulmann, Schrenss and Schamberg to be an effective detoxicant against poisoning with heavy metals, the author previously noted the positively beneficial effect in clinical cases of lead poisoning. He now reports his observations on the influence of this drug on experimental lead poisoning in rabbits. He first produced poisoning by injection of lead acetate, 5 per cent, in the proportion of 1 cc. per kilogram of body weight, and after the appearance of toxic effect, as viewed by a study of the blood, injected a 10 per cent solution of sodium thiosulphate in increasing doses. From these experiments, he concludes that the drug is effective in detoxication against lead poisoning, but its administration must be early in order to be absolutely sure of realizing therapeutic purpose.

KATO, Chicago.

BLOOD GROUPS OF THE JAPANESE, WITH A STATISTICAL STUDY AND GROUPING OF TWINS. K. OSHIDA, J. Pediat. (Tokyo), June 20, 1931, no. 373, p. 814.

The author typed the blood of 2,309 babies in the Red Cross Hospital maternity service, and found the percentage distribution to be: O group, 29.4 per cent; A group, 40.1 per cent; B group, 21.3 per cent, and AB group, 9 per cent. The author compares her results with those published by eleven other investigators, and average percentage figures for the combined examination of 15,319 persons are: O group, 31.3 per cent; A group, 37.8 per cent; B group, 20.0 per cent, and AB group, 9.9 per cent. She performed Wassermann tests in most of her cases, and found no definite relation between the blood types and the reaction. She also examined the types in 21 pairs of twins born in the maternity service of the hospital and compared them with those of their respective parents. All the twins showed the same blood type, whether uniovular or biovular. In the 179 examinations of the types of babies and their mothers, 51.4 per cent were of the same type, while 48.6 per cent were different.

KATO, Chicago.

HEREDITY AND THE UNIVERSAL BIOLOGIC SIGNIFICANCE OF BLOOD GROUPING. BERGAUER, Časop. lék. česk. **68**:365 (March 15) 1929.

A short summary of the history of isohemagglutination is followed by a review of the observations of various authors. Group characteristics are inherited according to mendelian expectation. Sex is not a factor in the heredity of group characteristics, which may be one of three heterozygotes or three homozygotes. The attempts to group various strains tends toward the theory of the polyphyletic development of man. Serologically the anthropoid apes and certain human strains show similar characteristics not found in some other apes. This is another argument for evolution.

STULIK, Chicago.

Society Transactions

NORTHWESTERN PEDIATRIC SOCIETY

ALEXANDER STEWART, M.D., *Secretary*

July 11, 1931

SAMUEL AMBERG, M.D., *Presiding*

THE WHOOPING COUGH PROBLEM. DR. L. W. SAUER.

The etiology, mode of dissemination and laboratory diagnosis of whooping cough are well established. It is the most prevalent communicable disease of early childhood, mainly because it is customary to procrastinate about diagnosis and quarantine until the whoop has developed. As in measles, the most contagious period is the catarrhal stage, i. e., before the clinical symptoms are typical. To make an earlier diagnosis possible, mother and physician must become whooping cough "minded." The cough plate of Chievitz and Meyer is comparable to the culture in the diagnosis of diphtheria. The plate must be exposed relatively early and must be well coughed on; it requires three or four days' incubation. Patients do not always exhale pertussis bacilli. A child may have typical paroxysms without expelling B. pertussis on the plate. It is best to expose plates in duplicate. A negative plate does not exclude the presence of pertussis.

Leukocytosis, especially lymphocytosis, characterizes the spasmodic stage, but is usually absent early in the catarrhal stage. The earlier in the course of the disease the patient is seen, the less characteristic is the cough, and the lower the blood count, but the more likely is the cough plate to be positive; the farther along the disease, the more typical is the cough and the higher the count, but the less likely will be the isolation of B. pertussis. The mortality rate is 1 per cent of patients of all ages, and 33 per cent of infants under 1 year.

Fresh, not cold, air, proper food and aseptic nursing care are essential; quinine, phenobarbital and ether administered rectally are valuable adjuncts that help give symptomatic relief. Vaccine therapy, as used at present, is of doubtful therapeutic value.

DISCUSSION

DR. MAX SEHAM: I have two questions. Dr. Sauer spoke of using ether per bowel. I wonder if he ever uses ether intramuscularly, and if so what effect it has. About what time does he feel that a diagnosis of whooping cough can be made, and at what time does the patient no longer transmit the disease?

DR. L. W. SAUER: The only way I have given ether is in oil by rectum, using a 20 per cent solution and giving, according to age, from 2 to 6 Gm. twice a day, preferably after an evacuation. I have not given ether by mouth or intramuscularly. According to some physicians, there is some danger of necrosis. In regard to the cough plate as an aid, I think it is wise to quarantine children as early as possible, because after the whoop is well established the cases are relatively harmless. After two weeks in the paroxysmal stage, the children are only slightly dangerous, except once or twice during the day. In fact, in Chicago, the health department has now made a rule that lifts quarantine three weeks after the first paroxysm, at which time the child wears an arm band and is allowed to leave the premises.

EXPERIMENTAL GLOMERULONEPHRITIS. DR. H. F. HELMHOLZ.

Demonstration was made of glomerular changes produced by three injections of streptococci at monthly intervals isolated from patients with subacute bacterial endocarditis. The changes were very evident in four of seven animals in which injection was made, but were not found until six months following the first injection.

The changes are characterized by hyaline changes in the glomerular tufts, adhesions between tuft and capsule and, in several cases, crescent formation. The glomerular involvement varies from 30 per cent in the less severe cases to 95 per cent in the most marked. In two animals in which one kidney or part of a kidney was removed and the animal killed some months later, a comparison of the sections showed that there had been a progressive development of the glomerular lesions.

DISCUSSION

DR. L. W. SAUER: Were there any other lesions in any other parts of the body?

DR. H. F. HELMHOLZ: There were practically no lesions elsewhere in the body. There were in the last case infarcts of the papilla in both kidneys which were apparently of very recent origin, as the tubules could still be made out as well as a very narrow zone of inflammatory demarcation. We did not find, as we had expected, lesions on the heart. We have injected additional cultures into about forty animals, and of these perhaps ten have died.

DR. L. W. SAUER: Do the kidneys in the cases of endocarditis show lesions?

DR. H. F. HELMHOLZ: Barnes of New York has described lesions somewhat similar to this. His pictures show collections of fibroblastic cells at the point of entrance of the capillaries into the glomerular tufts. In his article he has some excellent illustrations that show the hump formation, but do not show the typical adhesions.

DR. L. W. SAUER: When intramuscular injections are given, how long could there be a localized area of infiltration?

DR. H. F. HELMHOLZ: About four weeks, that is, from about three to six weeks before the lesion was entirely healed. Not all of the lesions broke down.

DR. L. W. SAUER: Would the excision of the one kidney and then a long time interval be a factor in the change?

DR. H. F. HELMHOLZ: We have removed a number of kidneys as controls. The only change is that the remaining kidney is somewhat larger in size. The kidneys in this particular study showed considerable sclerosis, and the lesions we found were not as marked in the remaining kidney as they were in the animal that had its kidney removed after about 245 days. One animal died in 320 days with both kidneys in place. However, the animal with the one kidney had the more typical lesions.

FURTHER EXPERIMENTS WITH REGARD TO PROTECTION AGAINST THUJONE CONVULSIONS. DR. H. M. KEITH.

In a previous paper a method was described for producing convulsions in rabbits. It consists of the intravenous injection of a normal convulsing dose, from 0.35 cc. to 0.4 cc. for each kilogram of body weight of a 1 per cent suspension of thujone in 6 per cent acacia. It was pointed out that animals that have not been used for this sort of work before must be used for each experiment, and that, in agreement with the conclusion of Lennox and his co-workers, groups of animals must be used instead of a single animal and the results considered statistically. The effect of dehydration and of three different acetone bodies on the production of convulsions were noted.

Since this paper was published, I have obtained a supply of β-hydroxybutyric acid (Eimer and Amend, New York) and have carried out an experiment similar to those previously described. It was found that the β-hydroxybutyric acid did not have any appreciable effect in preventing convulsions or altering their severity. The injection of this material was apparently accompanied by pain, as the animals always struggled and jerked their ears. It had no definite anesthetic effect.

The anticonvulsive effect of diacetone alcohol when given by stomach tube was also determined; 0.5 cc. of the alcohol diluted with distilled water was given for each kilogram of body weight. The animals were tested with thujone at intervals of one, five and twenty-four hours. There was little anticonvulsive effect within an hour; the effect was definite in five hours, but in twenty-four hours it had worn off considerably. In order to compare this effect with that of phenobarbital, 50 mg. of phenobarbital sodium for each kilogram of body weight was given by stomach tube. In one hour a definite anticonvulsive effect occurred; this was rather more marked at the intervals of six and twenty-four hours. The dose caused drowsiness in six hours, but it was noted that the animals were very irritable and objected to further handling or injection. This particular reaction was not noted in animals that received diacetone alcohol. The experiment was repeated, 25 mg. of phenobarbital sodium being used for each kilogram of body weight. The effect was, of course, less than that with the larger dose. The most marked anticonvulsive effect was noted after six hours. A much larger dose of phenobarbital sodium was also given, namely, 500 mg. for each kilogram of body weight; this amount was equal to the amount of diacetone alcohol used. The animals promptly became comatose; convulsions did not occur on the injection of thujone, and the dose proved lethal in twenty-four hours.

In a paper by Walton, Kehr and Loevenhart in 1928, the effect of diacetone alcohol was noted on rats and rabbits. It was stated that the maximal dose tolerated by rats was 3 cc. for each kilogram of body weight. I was able to show that this held true for rabbits also. Of six rabbits that received 3 cc. for each kilogram of body weight, only one died, death occurring in six days. Of six animals that received 4 cc. for each kilogram of body weight, four died within forty-eight hours. The other two remained well. Diacetone alcohol in doses of 2 cc. or more for each kilogram produces a destructive lesion in the liver of rats without any marked signs of toxicity. The lesion consists of partial destruction of the hepatic cells without injury to the biliary system and without definite localization in the central or peripheral portion of the lobule. These studies are not complete; further details will be reported later.

DISCUSSION

DR. I. MCQUARRIE: What is the mechanism of the convulsions with thujone? What happens?

DR. H. M. KEITH: There have been a great many studies of experimentally produced convulsions. I have made a special study of this for a long time. It is generally agreed that the drug causes stimulation of the cerebral cortex, although certain experimenters state that they can obtain convulsions with larger doses after the cortex has been removed. The convulsions are both tonic and clonic, and begin within from thirty to forty seconds after the administration of thujone.

HYALINIZATION OF GLOMERULI AND CAPSULES OF THE KIDNEYS OF INFANTS AND OF THE NEW-BORN. DR. S. F. MORGAN.

In 1909, Herxheimer described hyalinization of glomeruli and capsules of the kidneys of the new-born and of infants. His sections were stained with van Gieson's stain, and he emphasized that the hyaline part stained a bright red, with none of the yellow tint seen in adult tissues. Herxheimer reached the conclusion that he was dealing with irregularities of the kidney or a minimal anomaly of development.

Of twenty-eight patients studied, twenty-two were under 3 days of age, including nine premature infants and ten who were stillborn. The ages of the other six ranged from 10 days to 11 months. Four of ten sections of each kidney were studied with van Gieson's stain. Some of the sections contained fewer glomeruli, and therefore the material for study was not uniform. This study was entirely limited to hyalinization of glomeruli and capsules. In some cases there was an increase in connective tissue fibrils forming a fibrillar structure. We accepted these as hyaline, and in this study they are called questionable.

Of twenty-two infants under 3 days of age, we were able to show hyalinization in eight, or 36 per cent; in four it was questionable, and ten showed no hyalin. Of the ten stillborn infants, only one showed hyalinization of the glomeruli. Of the nine premature infants, four had a small amount of hyalin. In all of the six infants over 3 days of age, there were from a few to numerous areas of hyalinization. This is in agreement with Schwartz' finding that hyalinization occurs more frequently in the older patients. There was a history of infection in four of our cases. Again, in agreement with Schwartz, we found that all of these cases had a larger number of glomeruli hyalinized.

In our cases the number of glomeruli hyalinized was small, and usually the hyalinization was limited to a few loops. In only one instance was more than one half of a glomerulus involved, and no glomeruli were completely hyalinized. In the younger patients this happened more frequently.

From the data of Schwartz as well as from ours, we feel that it is better to withhold judgment as to the causes of this condition. However, the few and rather minute lesions found in stillborn infants and infants a few days old make the view of Herxheimer, that these are minimal anomalies of development, rather attractive.

Some Experiments with Intracutaneous Injections of Dyes. Dr. Samuel Amberg.

Keller advanced a hypothesis that water travels to the cathode in an electric field, and that this electrical factor of water transport is important biologically.

Dyes have been used to differentiate in tissues of animals and plants regions of greater and lesser electric negativity, that is, cathodal or anodal regions. Various factors have to be kept in mind, such as the possibility of the change of migration in different mediums, the production of colorless compounds by reduction or carbinol formation, the degree of dispersion and the power of causing irritation. All dyes used are water-soluble, and lipoid solubility and chemical constitution are not of much importance here.

Dyes are selected from a list given by Keller as cathodal or anodal. The objective was the differentiation of a tissue in vivo in the sense in which Keller used intradermal injections and noted the time of appearance. The tests were made on volunteers with 0.2 cc. of a 1:10,000 dilution of the dyes in salt solution. Of the cathode dyes the following were used: congo red, fluorescein, eosin, erythrosin, rose bengal, trypan red, alkali green, fuchsin, fuchsin acid, water blue and alkali blue, and of the anode dyes: malachite green, fuchsin basic, dahlia, brilliant cresyl blue, neutral red, methylene blue (methylthionine chloride, U. S. P.), safranin and acriflavine neutral.

I have no data about the distribution of the dyes in the skin, and so far as these rather rough experiments go, it has been impossible to arrive at a sharp differentiation. Aniline green proved to be very irritating, and neither methylene blue, fuchsin acid nor fuchin basic was changed to the colorless form. Litmus introduced intradermally into the skin showed blue, and the specimen at our disposal, though purified, was irritating.

Coarctation of the Aorta. Dr. J. B. Gillespie.

I shall report a case of coarctation of the aorta in a boy, aged 13 years, who was at the Mayo Clinic in September, 1930. He had had the ordinary diseases

of childhood; four months prior to admission he had had influenza, and he gave a history of a similar illness three months before that. He had had his tonsils and adenoids removed. He had complained occasionally of pains in the calves of the legs, his mother calling them growing pains. The family history was unimportant.

He had apparently been well, until during physical examination for football in 1930 the family doctor found the blood pressure above normal range. At that time the boy complained that his legs felt as though they did not want to come along with him. A diagnosis of malignant hypertension syndrome was made. On examination at the clinic in September, 1930, he appeared well developed and well nourished. His weight was 88½ pounds (40.6 Kg.), and he was 68 inches (172.7 cm.) tall. The pulse in the vessels of the upper extremities and trunk was easily obtained, but below the midline no pulsation could be obtained. The radial and ulnar pulse was good. The femoral pulse was grade 2 on the basis of 4. The blood pressure in the recumbent, sitting and standing positions was approximately the same, and the patient's lying on the right and left side seemed to have little effect on it. Physical examination showed that the pulsations in the intercostal arteries were full. The heart was somewhat enlarged and the aortic second sound accentuated. There was a systolic murmur. Examination of the eyes showed a constriction of the retinal vessels between the scapulae. There was moderate tortuosity, but no sclerosis. The Wassermann reaction was negative. An electrocardiogram was negative. A roentgenogram of the chest was negative, but it is questionable whether it was taken with the idea of coarctation of the aorta in mind. The McClure bleb test was done at the time, and it was found that the disappearance time from the leg was from twenty to forty minutes faster than that from the arm. This was of interest, because it may be recalled that reports on this test have credited the blood pressure as directly governing the disappearing time. Diathermy was instituted in the hospital in the hope of opening the vascular system. It was applied by means of electrodes and was given over the lumbar region in back and over the upper part of the abdomen for forty-five minutes twice daily. By the use of diathermy it was found that there was a marked effect on the temperature of the hand. The skin temperatures were taken before and fifteen minutes after diathermy. Blood pressure was not much affected by diathermy, although there was a slight elevation of pressure in the legs. I have not given all the results here, but just sufficient to give an idea of the condition. The patient was discharged three weeks later and sent home, with the suggestion that the diathermy test be made at home under the direction of the family doctor.

In December of the same year the patient returned to the clinic. At that time examination of the eyes showed persistent constriction of the retinal vessels but no sclerosis. Urinalysis was negative. The blood urea was 32 mg. per hundred cubic centimeters, and at that time it was felt that by palpation pulsation of the abdominal aorta could be obtained. The capillaries of the nail folds of the toes and fingers were examined, and the capillaries of the finger-nail folds were a little less numerous than usual, but the flow was normal. The capsules of the toe-nail folds were decreased in number, and the flow was markedly diminished. Reports from the family doctor since the patient returned home are that he is doing very well. His general appearance is improved, and he is feeling better. He was sent home on a regimen of restricted activity, and he is now playing a little golf and doing a few other things in the way of exercise, and the blood pressure is easily obtained.

The case is of particular interest for two reasons. Coarctation of the aorta and malignant hypertension have vastly different prognoses. The other interesting factor was the effect of diathermy on increasing the blood flow. On the upper extremities there was practically no effect, and on the lower extremities a rather marked effect. Rectal temperature and oral temperature were not affected by diathermy.

DISCUSSION

DR. G. R. TAYLOR: What do you think is the cause of the condition? Is it congenital?

DR. J. B. GILLESPIE: My experience with coarctation of the aorta is limited to one case that I saw at the University of Minnesota while with Dr. Bell. The condition is thought to be a developmental defect. Necropsy on a boy about 20 years of age showed an accompanying cirrhosis of the liver which was not explained by coarctation of the aorta.

DR. G. R. TAYLOR: Is the stenosis at a distance from the heart?

DR. J. B. GILLESPIE: Yes.

CONGENITAL FAMILIAL PTOSIS. DR. R. E. CUTTS.

I have here three cases of congenital ptosis in one family. There are four children in the family, one of whom does not show the condition. The father also has congenital ptosis to a less extent, and his mother had the same abnormality. We do not know about the other members of the family, and have been unable to find out about them.

Diagnosis of the condition is usually made from the fact that it is present at birth, is continually present thereafter, is usually bilateral, is frequently associated with deficiency of one or more of the extrinsic eye muscles, and more frequently is associated with congenital epicanthus.

The pathologic picture is one of defective musculature. This may consist of defective development, adhesions of the muscles, abnormality of insertion, replacement of the muscles by connective tissue bands or complete absence of muscle.

The condition is transmitted as a dominant mendelian character. H. H. Briggs in the *Journal of the American Ophthalmological Society* (**16**:255, 1928) reported on a family tree comprised of 128 persons; in 6 generations 64 persons were affected and 64 were not affected. J. T. Dimitry in the *American Journal of Ophthalmology* (**4**:655, 1921) reported 38 people in 5 generations of 1 family, of whom 21 were affected and 17 were not affected.

DISCUSSION

DR. R. S. ANDREWS: Would the condition always have to be bilateral? Can it not be unilateral?

DR. R. E. CUTTS: Congenital ptosis is usually bilateral, occasionally unilateral.

HEART BLOCK WITH ADAMS-STOKES' SYNDROME. DR. L. A. ALDERSON.

A boy, aged 11 years, came to the clinic on Oct. 21, 1930, because of dyspnea, slow pulse and frequent attacks of fainting. The patient apparently had been in good health until three years before admission, at which time he had fainted in school while exercising. Numerous fainting attacks had since followed; they were usually precipitated by exercise. During attacks, the boy usually fell backward, became unconscious for from a few seconds to several minutes, and was somewhat confused when he recovered. He usually knew when an attack was to occur. There were no convulsions. When he arose in the morning, he felt dizzy and sometimes fainted. The attacks occurred less frequently in the summer months. Exercising and climbing stairs caused dyspnea, but there was never any evidence of cyanosis. The pulse rate ranged between 45 and 50.

On general examination, the boy appeared to be in good health. The heart was slightly enlarged to the left. A systolic murmur was heard best at the apex, but was also heard over the entire precordium. The pulse rate varied; 46 and 36 were noted on palpating the apex beat. The systolic blood pressure was 125, and the diastolic 65. The Wassermann reaction of the blood, the Pirquet test, and urinalysis were negative. Hemoglobin was 90 per cent. Erythrocytes numbered

5,000,000, and leukocytes, 8,700, with a normal differential count. Roentgenograms of the head and thorax were negative. The basal metabolic rate was —14 per cent.

Electrocardiographic examination revealed: ventricular rate, 35; auricular rate, 70, and complete auriculoventricular dissociation with aberrant Q-R-S complexes. There was a marked left ventricular preponderance.

A diagnosis was made of heart block with Adams-Stokes' syndrome. The patient was given thyroid extract and small doses of tincture of belladonna. It was found necessary to discontinue medication in November, 1930, as attacks were more frequent. He has been doing well, but continues to have occasional fainting attacks.

We have noted only two references to Adams-Stokes' syndrome in children in the past ten years.

DISCUSSION

DR. I. MCQUARRIE: Had this boy had any rheumatic fever?

DR. L. A. ALDERSON: There was no history of rheumatic fever. In the literature, congenital heart disease and whooping cough were given as causes of heart block. I could find only two instances in the literature of Adams-Stokes' syndrome, one in a Dutch journal and the other in a Spanish journal. In one case the paternal grandfather had a very slow pulse rate, and the father of our patient had a pulse rate of 64 at the time of the examination of the boy.

CHICAGO PEDIATRIC SOCIETY

Regular Monthly Meeting, Oct. 20, 1931

HENRY E. IRISH, M.D., *President, in the Chair*

SURVEY OF THE PERSONNEL OF A CHILDREN'S HOSPITAL IN REGARD TO SCARLET FEVER, INCLUDING PROPHYLAXIS AND COMPARATIVE STUDIES OF SPECIAL BACTERIOLOGIC AND SEROLOGIC METHODS. DR. SILBER C. PEACOCK, MARIE WERNER (by invitation) and CHARLOTTE COLWELL (by invitation).

From 72, or 28 per cent, of 258 adults examined, hemolytic streptococci were isolated, and 45, or 17 per cent, gave a positive reaction to the skin test.

Forty of the 45 with positive skin tests received toxin for immunization. Of those retested, 87.5 per cent were immunized to the point at which they showed negative reactions to the skin test.

On the basis of both time off duty and symptomatology, 15 per cent of the people immunized experienced severe reactions. Approximately 85 per cent of the subjects receiving injections of toxin had more or less distinct reactions.

At the end of twenty-eight days hemolytic streptococci disappeared from the nose and throat of 92 per cent of the persons included in the survey. Only 15 per cent of susceptible persons, as determined by the Dick test, harbored organisms. Among the 258 people examined approximately the same number in the two groups (those with tonsils and those without them) had positive or negative cultures.

The erythema produced by the skin test averaged 19 by 18.6 mm. in diameter; its size bore no particular relation to the grade of reaction experienced by the adult immunized.

Of the adults who gave negative reactions to the skin test, 70 per cent gave no history of having had scarlet fever; 24 per cent gave a history of having had the disease, and 6 per cent furnished records without data on that question.

If the chocolate agar is a reliable means of differentiating nonscarlatinal from true scarlet fever streptococci, then 56.9 per cent of the organisms isolated in our series should be classified as related to scarlet fever.

If the opsonification test is of differential value, 43 per cent of the organisms isolated were of scarlatinal origin, an agreement of 80 per cent with those giving no reaction on chocolate agar.

Among the 186 people giving negative Dick tests, no definite case of scarlet fever developed. Among the 40 adults giving positive skin tests, scarlet fever developed in 2 before the series of immunizations were completed, and in none after the immunizations were completed. Among the 5 persons who were not immunized severe attacks of the disease occurred in 2.

THE CONTROL OF AN OUTBREAK OF SCARLET FEVER: A REPORT. DR. MAURICE L. BLATT and DR. MAURICE L. DALE (by invitation).

In all, 176 children, 30 nurses, 58 mothers and 7 male attendants constituted a group of 271 residents of St. Vincent's Infant and Maternity Hospital during an outbreak of scarlet fever. The disease was controlled in forty-eight hours by masking all adult attendants, taking cultures from all throats for the purpose of finding hemolytic streptococci and isolating all children harboring hemolytic organisms in their throats. The Dick test was performed on all the members of the personnel. Those with positive Dick tests were immunized with Dick toxin, and those intimately exposed to the most recent patient with scarlet fever were passively immunized.

After immunization negative results were obtained after five injections of Dick toxin in all but a single case, that of a nurse who showed a negative reaction after the sixth injection.

Of the 46 persons who were actively immunized, 28 had fever; 14 vomited; 2 had sore throats; 32 a mild local reaction; 6 a severe local reaction, and 1, a generalized scarlatiniform eruption.

The outbreak extended over a period of six weeks. The last four cases occurred within a period of seven days; the final case was diagnosed three days after control was attempted but before immunization had been started.

The institution was not closed to patients at any time.

EFFECT OF TONSILLECTOMY AND ADENOIDECTOMY ON THE SHICK REACTION (DIPHTHERIA IMMUNITY). DR. JOHN A. BIGLER.

Clinical evidence points to a decreased incidence of diphtheria in children on whom tonsillectomy has been performed. Shick tests were made on a large group of children just before tonsillectomy, and those who reacted positively were asked to return six months after tonsillectomy for a retest. Of 470 children who had not received active treatment for the production of immunization against diphtheria and who had not had diphtheria or received diphtheria antitoxin, 325, or 69 per cent, gave positive reactions to the Shick test, and 145, or 31 per cent, gave negative reactions just before tonsillectomy. Six months after tonsillectomy, 191 of the 325 with positive tests returned; of these, 176, or 92 per cent, still gave positive reactions and only 15, or 8 per cent, negative ones. The children who had received treatment for the production of active immunity against diphtheria, those who had had diphtheria and those who had received antitoxin because they were exposed to diphtheria, were suspected of having had diphtheria or were carriers of the bacillus were all put in separate groups. The results of the Shick test made on the children of these groups coincided closely with those already given.

The conclusions from the study on this series of children are: 1. Adenoidectomy and tonsillectomy had very little influence in changing a positive Shick reaction

to a negative one within from six to nine months after operation. 2. The small amount of toxin in the Shick test had little influence on the development of immunity to diphtheria as measured by the Shick test made after a period of from six to nine months after tonsillectomy, except possibly in the children who had received toxin-antitoxin for purposes of immunity and those who had had diphtheria and were treated with antitoxin. 3. It would seem that the decreased incidence of diphtheria after tonsillectomy is not due to increased immunity to diphtheria as measured by the Shick test, but to the removal of a portal of entry or of a fertile soil for the diphtheria bacilli.

DISCUSSION

DR. MAURICE DALE: I have a little additional information to present. After making Dick tests and immunizing the children with positive reactions as Dr. Blatt has described, we waited for six months and repeated the process in order to discover any other susceptible patients. In the course of this work some interesting findings appeared. Fifty-six infants of the original 176 tested were still in the hospital. Of these, 43 had given negative reactions and 13, positive ones. Those with positive reactions had been immunized and had given negative reactions a month after immunization. At the recent tests, in 6 of the original 56 the reaction had become positive again. One of the 6 was one of the 13 who had been immunized at the age of 5 months, and at 11 months the reaction was positive again. The other 5 had originally given negative reactions to the Dick test. Their ages at the first test were 12, 12, 5, 4 and 2 months. One of them with a negative test at 12 months showed a faint positive reaction at 15 months and a strong positive reaction at 18 months.

DR. JESSE R. GERSTLEY: Dr. Peacock said that in some of these patients the hemolytic streptococcus disappeared from the throat within twenty-eight days. To me, at least, he did not make clear whether this was a casual observation on the patients recovering from scarlet fever in the ward or whether the disappearance of the streptococcous was related to inoculations of scarlet fever toxin.

DR. HENRY E. IRISH: I should like to ask both Dr. Peacock and Dr. Blatt what preparations were used in the immunization of the patients. Were they commercial or special products?

DR. A. I. LOVE: I should like to know whether Dr. Blatt took cultures from the throats of adult nurses who gave positive reactions, with control of the condition. How long did the attendants wear the masks, and did their reactions become negative? Did Dr. Blatt take cultures from the throats of attendants and nurses? How long did they wear the masks?

DR. GUSTAV L. KAUFMANN: I am rather interested in the discussion as bearing on the discussion that occurred last week in Cincinnati, when Dr. R. A. Lyon reported a series of cases in which he used combined formaldehyzed diphtheria and scarlet fever toxins. He gave three injections, one every three weeks. He reported 100 per cent negative Shick reactions and 88 per cent negative Dick tests.

DR. C. A. ALDRICH: I should like to know the incidence of sore throat without rash in the institutions. It seems to me that this is one of the big questions in the immunization against scarlet fever. One may immunize against the exanthem and not against the scarlet fever throat. If any one could tell us about the cases in which the patients had sore throat that might have been due to scarlet fever, but in which a rash did not occur, it would be valuable.

DR. I. M. LEVIN: The striking appearance of diffuse scarlatinal-like eruptions following the injection of scarlet fever toxin for active immunization, as mentioned by the essayists, has been investigated by Toyoda and his collaborators (Scarlet Fever, AM. J. DIS. CHILD. **41**:1010 [May] 1931). They showed that "the artificially produced general rash is identical with the rash of scarlet fever as demon-

strated by the fact that the area of skin that had been treated with the serum of a patient convalescing from scarlet fever and with scarlatinal streptococcus antitoxin before the injection of the toxin was entirely free from the rash."

Further they pointed out that in evaluating the Dick test, the two components of the Dick toxin (heat-labile exotoxin and heat-stabile endotoxin) must be considered. "Pure heat-labile exotoxin contains no nitrogen, and is easily destroyed at a temperature of 80 C. maintained for half an hour. The symptoms of scarlet fever in its early stage are all caused by this toxin. The cutaneous reaction to this toxin is pronounced in persons not immunized against streptococcus toxin or scarlet fever, and never causes an allergic reaction. On the contrary, heat-stabile endotoxin is not destroyed even when kept at 100 C. for two hours. The cutaneous reaction to this toxin is often found to produce an allergic reaction in those immunized against streptococcus or scarlet fever. As the various drawbacks to the use of the Dick test are traced to the heat-stabile endotoxin that it contains, the toxin employed for the test should be the pure heat-labile exotoxin mentioned. Otherwise the results of experiments by different workers cannot be expected to coincide."

In employing the Dick test were these facts taken into consideration by the essayists?

DR. SILBER C. PEACOCK: Squibb's commercial toxin was used both for the skin tests and for the immunization in our work. It was our aim to be as practical as possible in this investigation.

DR. MAURICE L. BLATT: I knew nothing of the contents of Dr. Peacock's paper until this evening, but if he and I had collaborated on this work, we could not have approached it more nearly from the same point of view. I did not consult the Dicks as to how scarlet fever should be controlled, and I used the Squibb products bought in the open market. My associates and I followed the instructions as laid down by the Dicks in their contributions to the literature and included in the pamphlet that accompanies the Squibb product.

One fact that I did not bring out particularly in my paper was that we used an antiseptic in the noses and throats of the children and adults having positive hemolytic cultures. I have asked the executive committee to have the society meeting at St. Vincent's in March, and I hope at that time to present the data on this work. We had no controls on this nasal treatment, so I did not mention it in the paper, but Dr. Peacock has done something for which I am extremely grateful. He has a group of controls which I hope to utilize.

The longest period before the streptococcus disappeared permanently from the nasopharynx was eighteen days in children and twenty days in adults.

As to sore throats without a rash, we were looking for them all the time and found none. At the time of this investigation, the resident physician associated with me and Dr. Dale made daily rounds. The visiting staff also visited the wards two or three times a week. The staff was on the lookout for suspicious cases, but during this time there were none.

Among 170 people, we might believe that another case had occurred, except for the measures instituted. It is another test of the efficacy of prophylaxis. My problem was to control an epidemic, and this paper is a report of that control. We masked all adults until cultures from their throats had been taken, and we isolated all the children with positive cultures in rooms together and proceeded with the treatments for the throat. A definite chronological line apparently related to our prophylaxis appeared. No cases have occurred since then.

We are retesting as many of the group as remain in the institution and reimmunizing those with positive tests. This is the end of the first six-months period. We plan to continue testing and immunizing at this interval. A further report will have no value, however, until scarlet fever again assumes epidemic proportions in Chicago, which should be in 1936.

NEW YORK ACADEMY OF MEDICINE, SECTION OF PEDIATRICS

Nov. 12, 1931

HERBERT B. WILCOX, M.D., *Presiding*

A THIRTEEN DAY OLD INFANT SUCCESSFULLY OPERATED ON FOR CONGENITAL DIAPHRAGMATIC HERNIA. DR. ABRAHAM TOW.

A girl, aged 13 days, had been successfully operated on for congenital diaphragmatic hernia. Delivery was normal. The birth weight was 6 pounds and 4 ounces (2,836 Gm.). On the morning of the seventh day she had an attack of marked cyanosis. Dextrocardia was present without situs inversus. On this basis a roentgenogram was taken to confirm the diagnosis of diaphragmatic hernia. The cyanosis gradually grew worse as more and more of the intestine entered the left side of the chest. The wall of the chest bulged more anteriorly. Breath sounds became absent, and percussion was tympanitic. Dr. Coryllos operated on the patient. Thoracotomy was done without rib resection. All of the small intestine, cecum, transverse colon, part of the descending colon and all of the spleen were in the chest. Reduction was impossible, and the incision was prolonged on the abdominal wall. The reduction was accomplished by working from above and below the diaphragm. The postoperative course was stormy, but the patient finally recovered. The use of oxygen and carbon dioxide as high as 10 per cent for the first two days was emphasized to prevent the development of massive or patchy atelectases which is the forerunner of postoperative pneumonias. At the age of 3 months, the patient weighed 9 pounds and 9 ounces (4,350 Gm.) and was in excellent condition.

DISCUSSION

DR. E. J. DONOVAN: I should like to congratulate Dr. Tow and Dr. Coryllos on this most remarkable result in a baby 13 days old. In a superficial search of the literature I have seen no case reported in which surgical treatment was given as young a patient as this baby.

It seems to me that diaphragmatic hernia is being found more frequently of late, and one is impressed by the number of articles that have been published on this subject. There is perhaps no condition in which the roentgenogram has played so great a part in making a difficult diagnosis simple. Before the roentgenogram, Lichtenstein collected 250 cases of diaphragmatic hernia, and in only 5 was the diagnosis made clinically.

The first cases were those reported in 1610 by Ambrose Paré. One of the earliest and, perhaps, most comprehensive papers on the subject was written by Sir Ashley Cooper in 1824. One of the largest series in this country in recent years was that of Hedblom, reported in 1924. He reported 378 cases, 19 from the Mayo Clinic and 359 from the literature. There were 22 patients under 10 years of age in this series. A clinical and roentgen diagnosis was made in 59 per cent of the cases. Several of the patients had been operated on previously and a diaphragmatic hernia had not been recognized.

Diaphragmatic hernia may be either congenital or acquired, most of the acquired types being the result of direct trauma. The congenital type in most large series is between 10 and 14 per cent. Of the congenital type, there are two main varieties, hernias passing through an enlarged esophageal opening and those passing through a defect in the diaphragm. Bilateral cases have been reported. The majority of the cases do not show a true sac, it being found in only 24 of Hedblom's 378 cases.

Almost every abdominal structure has been found in the thorax; there have been 4 cases in which even the pancreas was involved and 1 in which the left kidney was found.

I have seen 7 cases in the past year, 2 of them in adults, 68 and 55 years of age, respectively. I mention these cases only to show that a patient may have a diaphragmatic hernia, even of congenital origin, and reach adult life without many symptoms. This applies particularly to hernias through the esophageal opening when the stomach only is involved. Almost all of the cases involving the large or small intestines show intestinal obstruction sooner or later.

The remaining 5 patients were children, the oldest a boy of 6 years with a diaphragmatic hernia on the left side showing several loops of small intestine in the thorax. He had frequent acute attacks and digestive disturbances. Operation was refused by the parents.

The next patient was a baby 6 weeks old whom I had the pleasure of seeing operated on in another hospital. This patient had a large defect in the left leaf of the diaphragm with a great part of the small intestine, colon and spleen in the thorax. There was so much of the left lobe of the liver in the thorax that it was impossible to close the opening of the diaphragm satisfactorily. The child died two days later.

The next patient, a baby 10 days old, was admitted to St. Luke's Hospital in a moribund condition after a roentgenogram had been made in another hospital. The roentgenogram showed several loops of the small intestine and some of the stomach in the thorax. The child died within twenty-four hours of admission.

The next 2 patients I operated on at the Babies' Hospital. The first was 4 months old with a very similar case to that presented by Dr. Tow. Practically all of the small intestine and almost all of the large intestine, except the sigmoid and the spleen, were in the thorax, having passed through the left foramen of Bochdalecki. Reduction was accomplished through an abdominal approach, the opening was closed, and the child had a most uneventful convalescence. He is normal in every way now, one year after operation.

The other child was a girl 6 months of age. All of the stomach and part of the duodenum and transverse colon had passed into the thorax through an esophageal opening large enough to admit four fingers. The opening was closed, and the child progressed well for twelve days, when she had a gastric upset. At that time a roentgenogram showed that a small part of the stomach (one-sixth part) had gone back through the esophageal opening. She progressed well, gained weight, did not vomit and was sent home for further observation.

Surgically speaking, the approach to the diaphragm either through the abdomen or the thorax is difficult in an adult, and, of course, much more so in a child. If we make an incision through the thorax, we wish that we had gone through the abdomen, and if we go through the abdomen, we wish we had gone through the thorax. Dr. Coryllos is to be particularly congratulated on his way of handling this case, especially in so young a child.

DR. POL N. CORYLLOS: I shall be very brief, as the essential operative procedure that I followed was described in detail by Dr. Tow.

I would only like to mention the reasons that made me decide to operate on an almost moribund 13 day old baby. The arguments against the operation were: (1) the extremely young age; (2) the advanced degree of dehydration and the toxic condition because of intestinal obstruction; (3) the dyspnea and cyanosis due to the presence of the whole intestine in the left side of the chest, and the collapsed lung, and (4) the displacement of the heart completely to the right.

None of these arguments seemed to me prohibitive.

The extremely young age was rather in favor of the operation. The principal danger in this case was anoxemia, and it is known that young animals show much greater resistance to this condition than grown-ups. The dehydration and toxic condition were serious handicaps. The operation, however, was the only way to afford relief from them, and I do not think that any surgeon should hesitate to operate on a patient, however toxic, in presence of intestinal obstruction.

The most serious argument against an operation that would necessitate a wide opening of the chest was the very rapid pulse and cyanosis. On the other hand,

however, it was evident that circulatory and respiratory disturbances were due to the presence of the dilated intestine in the left side of the chest, which suppressed the intrapleural negative pressure, transforming it to positive, which brought about the inability of the left lung to expand, and pushed the mediastinum and the heart to the right. This being the fact, the opening of the chest thereby producing an open pneumothorax could not make the condition worse, and if the little baby was still alive with positive pressure in the left side of the chest, there was no obvious reason why it would not withstand atmospheric pressure in it. The mediastinum and the heart would not be more displaced to the right than they were already. Furthermore, intratracheal insufflation with oxygen and 8 per cent of carbon dioxide would eliminate any immediate danger of anoxemia.

The result justified this reasoning. The baby withstood remarkably well this rather extensive operation. The heart beats had been very rapid, around 160, but regular. I did not worry about the rapid pulse. Previous long experience in heart operations on the dog had taught me that fibrillation does not occur without previous slowing down of the heart. Only once did I run into serious danger. This was when both tanks of the anesthesia apparatus emptied, and the anesthetist being too much absorbed in the operation did not notice it immediately. The heart slowed down and showed some irregularity. This was quickly corrected, and the rapid, regular breathing was restored immediately after the administration of oxygen and carbon dioxide was resumed. I really think that the success in this case shows the paramount importance of experimental training and of knowledge of the physiology and mechanics of the chest in thoracic surgery.

As for the indications for operation in cases of diaphragmatic hernia in very young babies, I think that when the intestine is present in the chest cavity, the operation is imperative. It is the only chance for the patient; the age is of no importance. Any delay in these cases of false hernia makes conditions worse, because more intestine is aspirated, and the obstruction is increased. Dehydration and starvation, with acidosis and decrease in chlorides, rapidly undermine the resistance of the baby. It is not the same when only the stomach is present in the hernia. In such cases, we have to deal more often with true hernias, i. e., with conservation of the serosa covering, which opposes the rapid progress of the hernia; gastric dilatation and vomiting, if present, can easily be relieved by gastric intubation. Furthermore, in a number of cases reported in the literature, these gastric hernias were gradually reduced by themselves.

In closing, I want to add a few words on postoperative care and complications. Postoperative care consists in giving to the patient oxygen, water, chlorides and dextrose in sufficient amounts. The first is carried out by placing the patient under an oxygen tent for twenty-four or forty-eight hours. I wish to warn, however, against the danger of depriving the patient of carbon dioxide, thus producing apnea. The respiratory center of these patients is accustomed to a high concentration of carbon dioxide, so that from 6 to 8 per cent of carbon dioxide should be administered with the oxygen. Chlorides, dextrose and water should be administered by hypodermoclysis in amounts of 300 or 500 cc. for the first twelve hours.

As for the complications, the most important is: (1) pulmonary atelectasis and bronchopneumonia or pneumonia to which it opens the way, and (2) infection. The best way of forcing the lungs to expand is, on one hand, forcible inflation at the end of the operation, before closing the chest, and, on the other hand, aspiration of the pleural air after closure of the chest.

Accumulation of fluid in the chest is generally easily dealt with by tapping the chest. No drainage is necessary.

In terminating, I want again to congratulate Dr. Tow and Dr. Hawks on their diagnosis and to thank them for having asked me to cooperate in saving the ebbing life of this small patient.

DR. L. T. LE WALD: There are two types of hernia in which the patient should not be operated on unless there is complication by some intercurrent disease of the structures in the hernia. One type is that in which the stomach is entirely above the diaphragm, so-called "thoracic stomach." I have seen two cases,

one in a child and one in an adult. In this type the patient can well be kept under observation and not be operated on, as the esophagus is very short and will not permit the stomach to be placed entirely within the abdominal cavity. The other type of case is that in which there is a complete absence of the left half of the diaphragm. Two adults with this defect whom I took roentgenograms of showed no serious complications, as the opening is so large that the bowel does not become obstructed. In this type of case one can withhold operation, as it would be almost impossible for the surgeon to find material from which to make an entire left diaphragm.

DR. PHILIP STIMSON: It makes a good deal of difference in the treatment for diaphragmatic hernia whether the hernia is through the left or the right foramen of Bochdalecki. As early as 1911, Eppinger in Germany collected 635 cases, of which 580 were on the left side of the diaphragm, the other 55 on the right, left-sided hernias being, therefore, over ten times as common as those through the other side.

In 1923, a case through the right foramen was reported from the Cornell Clinic, the condition being diagnosed when the patient was 11 months old, with a weight of 12 pounds (5,400 Gm.). The greater curvature of the stomach was pulled through the opening into the chest. Operation was not considered advisable, and the child was treated medically, being deliberately spoiled so as to avoid crying. Many very small meals were given, and when 2 years old, the child appeared physically normal in weight and nutrition. Two years ago at the age of 8, a roentgenogram revealed an absolutely normal gastro-intestinal tract. The hernia was no longer present, and physical examination revealed nothing abnormal. Hence, particularly in right-sided hernias, it would seem that surgical intervention is not always necessary.

DR. ABRAHAM TOW: This case was presented to show that operation can be done at an early age.

A study of the statistics shows that the operative fatality is very great. A review would lead one to believe that often the patient comes to the surgeon in a poor condition. If the physician would be a little more prompt in turning over the patient to the surgeon, the operative results would be far better.

STUDIES ON THE MECHANISM OF ACUTE RESPIRATORY INFECTION. DR. ALPHONSE R. DOCHEZ.

Dr. Dochez reported observations extending over several years in acute infections of the upper respiratory tract. His studies included carefully controlled infections in human beings and monkeys. He described his methods of filtration of nasal washings, dilution and retransplant in these infections both in vivo and vitro.

DR. OSCAR SCHLOSS: Dr. Dochez' results are so clear-cut and definite that they do not admit of much discussion, particularly by one who is not a bacteriologist. They serve to throw considerable light on the rôle of a filtrable virus in initiating the common infectious cold. They also serve to reconcile a number of conflicting observations which point to different types of known bacteria as possible infecting agents. Dr. Dochez' hypothesis that the infection is perhaps initiated by the virus and that secondary invaders may be of importance in causing the continuance of symptoms and complications would seem important and would probably explain many clinical features of these infections of the upper respiratory tract, which are at present quite obscure.

We all know that these infections vary tremendously in severity, in different seasons, in different persons and in the same person at different times. It seems quite possible that this variation may be explained to some degree by the nature of the secondary infecting organisms — by their variation in virulence or the variation in the susceptibility of different persons.

It would seem to me that these observations would extend further than to the common cold. It is rather interesting that the infection can be initiated by one agent which prepares the soil for secondary invaders that may contribute to the symptomatology and complications of the disease. Probably this principle may serve as a starting point in the investigation of other obscure infections.

The work of Dr. Dochez and his collaborators offers tempting fields for speculation, but it seems to me best to avoid this question and to be satisfied with what Dr. Dochez has given and await the results of further investigations. It would seem, however, perfectly definite that these observations have furnished a guide to a clearer and more practical understanding of the common cold.

DR. A. R. DOCHEZ: I have little more to say except to draw attention to an interesting disease that has recently been studied by the Department of Animal Pathology of the Rockefeller Institute. This disease is called "swine influenza." In this disease two organisms, a filtrable virus and a hemophilic bacillus, act in conjunction to produce its typical severe manifestations. These consist many times in a fatal bronchopneumonia. It is a matter of great interest that each of the pathogenic agents concerned is relatively harmless when acting alone. We have made no studies concerning the persistence of the virus of the common cold in either water or oily suspensions.

SUSCEPTIBILITY PROBLEMS IN POLIOMYELITIS. DR. CLAUS W. JUNGEBLUT and DR. EARL T. ENGLE.

All epidemics of infantile paralysis have been characterized by three distinct features: (1) the strikingly increased incidence of the disease in children under 5 years of age; (2) the irregular spread of the epidemic in a given outbreak, and (3) the seasonal fluctuation which limits the epidemic waves to the late summer and early fall months.

Epidemiologic studies by the authors have disclosed that the age distribution in epidemics of poliomyelitis varies in direct proportion to the development of puberty in different countries. This may be taken to indicate the absence of a physiologic maturation factor as the main reason for the elective susceptibility of young children. Approaching the problem experimentally, the authors have found some evidence that this factor may be connected with a secretion of the anterior pituitary gland which governs the normal physiologic development and the function of other endocrine glands, particularly that of the sexual organs, the thyroid and the suprarenal cortex. It has been possible in a small number of experiments to protect immature monkeys against intracerebral inoculation of the virus after treatment with anterior pituitary extracts or implants, although the success has not always been uniform. Such animals after hormone treatment have exhibited physical signs of accelerated maturity, and their serum has occasionally acquired the power to neutralize the virus in vitro, a property normally absent in the serum of young monkeys and infants, but present in that of most adult human beings. The results obtained with normal adult monkey serums have so far been too irregular to permit definite conclusions, although neutralization has been observed in two instances. Our experiments suggest that the protection enjoyed by adult human beings is not due so much to latent immunization by contact with the virus, as was formerly believed, but rests primarily on the hormonal balance characteristic of adult life. The influence of the summer climate is possibly conducive in lowering the normal endocrine balance of certain predisposed persons, young or old, in such a manner that the resulting deficiency breaks down the resistance to the invasion of the central nervous system by the virus.

Further evidence as to an innate predisposition to the disease has been obtained from the study of blood group distribution in cases of poliomyelitis in collaboration with Dr. Lawrence Smith from the Willard Parker Hospital. It has been found that persons belonging to one particular blood group (group B) are apparently more resistant to the infection than members of the other three groups. Similarly, convalescent serums from persons of this group have been more potent in their virucidal effect than the serums from persons of the other groups.

This is a preliminary report.

(This work was conducted under a grant from the International Committee for the Study of Infantile Paralysis financed by Jeremiah Milbank.)

DISCUSSION

DR. E. T. ENGLE: My interest in this work has come about not because I am an immunologist, but because I am interested in the problems of puberty, especially in their endocrine relationships. You are perfectly aware of the fact that, historically speaking, one can divide the hormones into two groups; in the first group, consisting of insulin, thyroxine, pituitary, etc., are hormones, the properties of which are well known and which have well defined clinical usages; the other group has come into general attention only recently, containing the hormones of the gonads, of the anterior lobe and of the suprarenal cortex. Of these, only one, theelin, is known chemically and is produced commercially in pure form. For the remainder of this second group, we are dealing with rather impure extracts which are still in the laboratory stage.

The reason for having used the anterior lobe in these experiments dates back to the demonstration by P. E. Smith, in 1926, that hypophysectomy in the adult rat was followed by cessation of activity of the reproductive system and was also accompanied by a hypoplasia of the thyroid and the suprarenal glands. In subsequent studies with Smith on the active principle in the anterior lobe, it was shown that this was the one factor that was responsible for the structural and functional aspects of puberty. In the present work on poliomyelitis, Dr. Jungeblut and I have felt that a possibility existed, which he has discussed, that susceptibility to poliomyelitis in immature persons and infantile monkeys is a question of physiologic inadequacy. In the experimental field, we have felt that we could modify certain of these inadequacies by hormone treatment, and our results have shown that we have distinctly modified the course of the infection after experimental inoculation with the poliomyelitis virus.

It is known that in a normal adult person, especially during pregnancy but also during uncomplicated adult life, are to be found the active principles of the anterior lobe in the blood, and that the sex hormones have been recovered from the urine in the respective sexes. The hormone balance, while fluctuating, is constant, and its presence is recognized after adequate biologic tests. In these immature experimental monkeys, we are attempting to create in some measure the hormone balance that is normally maintained in the adult who is insusceptible to poliomyelitis infection. In this connection it should be emphasized that puberty is not a phenomenon of sudden appearance, but is one of slow physiologic maturation which begins about from the fifth to the seventh years in the child, and extends beyond the period of the first menses. This epoch is but an expression of a physiologic hormone balance which began in childhood and which reaches somatic expression only after the individual nears pubescence.

DR. RUSTIN MCINTOSH: We have all had a number of embarrassing moments this summer when we have been asked to explain the susceptibility of persons to poliomyelitis and the mechanism of resistance. To attempt an explanation along familiar immunologic lines has been difficult, and we have been confronted with a number of startling inconsistencies. We should welcome any challenge such as has been put forward this evening to reexamine our data and get a new point of view.

It has long been known that there is some relation between constitution and susceptibility to poliomyelitis. As early as 1911, Draper pointed out that children coming down with poliomyelitis tended to conform to a constitutional group, that is, they bore some physical resemblance to each other. It was pointed out at that time also that the constitutional type involved in poliomyelitis closely resembled that involved in meningococcus meningitis. The study of constitution has not been taken up with enthusiasm in this country because of lack of objective methods

of study. For many years, Draper and others have devoted a great deal of industry and ingenuity to the search for methods by which constitution could be studied in an entirely objective manner.

The evidence presented by Dr. Jungeblut and Dr. Engle this evening offers an interesting approach to the study of the relationship between constitution and susceptibility to infection, since it has already been proved that the endocrine organs play a part in the determination of constitution. These workers have introduced a methodology for an experimental approach to this whole problem. It should be emphasized, as has already been pointed out by Dr. Jungeblut, that these new conceptions may apply to many different types of infections, not merely to poliomyelitis. We may well accept their challenge to reexamine our conception of the mechanism of susceptibility. I trust that our acceptance of this theory will not take the form of rushing to the drug store to buy a bottle of tablets of pituitary extract. But we shall all watch the progress of this work with unusual interest.

DR. C. W. JUNGEBLUT: In concluding, I should like, perhaps, to add one other point which I forgot to bring out with sufficient emphasis. If the falling off of the morbidity in the older age groups, coincident with the development of normal virucidal substances, were due predominantly to actual exposure to the virus, we should be dealing with a fairly simple mechanism. However, there is nothing more difficult than to build up an artificial immunity in the monkey by various methods of active immunization. Dr. Hazen and I sprayed the nose and throat of monkeys for ten weeks with large doses of live virus without obtaining protection against intracerebral infection and without being able to detect any antibody response in the serum. In other words, the mechanism that has been alleged to produce insusceptibility in adult human beings cannot be reproduced experimentally in the monkey.

One other point that I should like to draw attention to is the apparent similarity in the production of normal virucidal substances against herpes virus, another neurotropic virus causing a disease that shares certain epidemiologic characteristics with poliomyelitis. Here again we know from the work of Dr. Gay and Dr. Holden that the vast majority of normal adult human serums neutralize the virus in vitro, while the percentage of neutralization is very much diminished with serum from patients suffering from herpetic or encephalitic infection. While none of the arguments discussed, taken separately, is probably sufficient proof to establish our hypothesis, I feel that the total weight of evidence coming from so many different angles would go pretty far in suggesting the implication of a deficiency factor in the susceptibility problem.

Book Reviews

Physiologie des Kindesalters. By Egon Helmreich. Volume 1. Price, 28 marks. Pp. 364, with 6 tables. Berlin: Julius Springer, 1931.

A description of the functions of the child's organism with special attention to the characteristics in which they differ from those of the adult forms the subject matter of this book. The general principles underlying the differences are discussed, and quantitative differences, expressed numerically where possible, are included.

The arrangement of the material is new and interesting. The author first discusses the transformation of energy, the ultimate goal toward which all life processes are directed. The three components that determine the energy requirement, that is, basal metabolism, specific dynamic action of foodstuffs and work, may be influenced by various factors: body surface, youth, growth, sex, proportion of breathing protoplasm, food intake, storage and exercise. Methods for estimating the nutritional requirements are briefly described.

The second section discusses fully the heat economy of the body: heat formation and control and the characteristics of heat regulation peculiar to the child under normal and abnormal conditions.

Under the heading "Metabolism" a separate and very complete discussion is given of the fate in the body of each of the various food elements, including vitamins, and of their significance in the growing organism. The fourth section describes the functions of the various systems: circulation, blood, respiration, digestion and excretion of urine. These are presented as "the servants of metabolism." This arrangement makes it possible to bring out the relationship of the separate functions to the general processes of metabolism and energy production. The last section is a bibliography.

The volume presents in compact form a very complete summary of the present knowledge of the life processes in the child. It is readable German and should be valuable to the pediatrician both for study and for reference. A second volume on "Animal Functions" will be published soon by the same author.

Health Protection for the Preschool Child. By George T. Palmer, Dr. P.H.; Mahew Derryberry, and Philip Van Ingen, M.D. Price, $2.50. Pp. 275, with 44 tables and 57 charts. New York: The Century Company, 1931.

This volume sets forth the results of the most extensive survey of its kind ever attempted and provides for the first time a national index of the extent to which we are protecting the health of our children during the very important period between birth and the sixth year of life.

The painstaking accuracy with which these studies were planned and carried through should provide a standard for future surveys.

The results are most illuminating and stress a point that the Section on Medical Service emphasized at its final session at the White House Conference in February, 1931, that one of our first important jobs in protecting the health of our children is to secure a wider application of well known procedures.

We read in the report, for instance, that the highest percentage of preschool children that have been immunized against diphtheria in any city in the United States is 50 per cent. What is still more illuminating is that at the other end of the list we find one city in which only 1 per cent of this age group has been immunized.

The figures are almost identical for vaccination against smallpox, the highest percentage for any city being 48 per cent, and the lowest, 2 per cent. This certainly indicates the necessity for application of the known.

It further points out to the pediatrician and the general practitioner who cares for children, as well as to health officers, hospitals and clinics, a definite responsibility.

It is the kind of information that will make this extraordinary study and illuminating report of unusual value to the groups to which reference has just been made.

Le paludisme et l'enfant. By Bureau d'encouragement pour l'emploi de la luinine. Pp. 75, with 22 figures. Lyon: Bosc. Freres & Riou, 1931.

This book was published by the society for the prevention of malaria. It gives first the prevalence of malaria in Africa and India, both in children and in expectant mothers. Prophylaxis and treatment are then discussed. Quinine, 5 mg. per hundred cubic centimeters, is advised for nursing mothers, as it is excreted in breast milk. Prophylaxis is best carried on by school propaganda. There are some interesting pictures of school children receiving quinine in Algeria. The book is interesting and contains a good bibliography on malarial therapy.

Criteria for the Interpretation of Electrocardiograms. By A. C. DeGraff. Price, 35 cents. Pp. 20, with 6 pages of illustrations. New York: New York Tuberculosis and Health Association, 1931.

This pamphlet has been prepared by the Research Subdivision of the Heart Committee of the New York Tuberculosis and Health Association. The key contains fifty standard conditions, their definitions and illustrated electrocardiograms.

Directory of Pediatric Societies

INTERNATIONAL

International Association of Preventive Pediatrics

President: Professor Taillens, Lausanne, Switzerland.
Secretary: Dr. P. Oltramare, rue Decandolle, Geneva, Switzerland.
Place: Geneva, Switzerland. Time: July 15, 1932.

International Pediatric Congress

President: Dr. George Frederic Still, 28 Queen Anne St., London, W. 1.
Place: London. Time: 1933.

NATIONAL

American Medical Association, Scientific Assembly, Section on Diseases of Children

Chairman: Dr. Jay I. Durand, 1305, 4th Ave., Seattle.
Secretary: Dr. Alfred A. Walker, Highland Plaza Apartments, Birmingham, Ala.
Place: New Orleans. Time: May 9-13, 1932.

American Academy of Pediatrics

President: Dr. John L. Morse, 319 Longwood Ave., Boston.
Secretary: Dr. C. G. Grulee, 636 Church St., Evanston, Ill.
Place: New Orleans. Time: June, 1932.

American Child Health Association

President: Hon. Herbert Hoover, Washington, D. C.
Secretary: Dr. Philip Van Ingen, 125 E. 71st St., New York.

American Pediatric Society

President: Dr. Howard Childs Carpenter, 1805 Spruce St., Philadelphia.
Secretary-Treasurer: Dr. Hugh McCulloch, 325 N. Euclid, St. Louis.
Place: Rochester, Minn. Time: May 26-28, 1932.

Association of American Teachers of the Diseases of Children

President: Dr. Ralph M. Tyson, 334 S. 21st St., Philadelphia.
Secretary: Dr. Oscar Reiss, 1930 Wilshire Blvd., Los Angeles.
Place: New Orleans. Time: 1932.

Children's Hospital Association of America

President: Dr. Joseph Brennemann, 707 Fullerton Ave., Chicago.
Secretary-Treasurer: Miss Bena M. Henderson, 721 N. 17th St., Milwaukee.

Canadian Society for the Study of Diseases of Children

President: Dr. G. A. Campbell, 164 Metcalfe St., Ottawa, Ontario.
Secretary-Treasurer: Dr. L. P. MacHaffie, 162 Clemow Ave., Ottawa, Ontario.

SECTIONAL

Central States Pediatric Society

President: Dr. Frank C. Neff, 406 W. 34th St., Kansas City, Mo.
Secretary: Dr. A. H. Parmelee, 715 Lake St., Oak Park, Ill.
Place: Kansas City, Mo. Time: Fall, 1932.

North Pacific Pediatric Society

President: Dr. A. Howard Spohn, 925 West Georgia St., Vancouver, B. C.
Secretary: Dr. L. Howard Smith, 734 Medical Arts Bldg., Portland, Ore.

Southern Medical Association, Section on Pediatrics

Chairman: Dr. Horton Casparis, Vanderbilt University Hospital, Nashville, Tenn.
Secretary: Dr. Luther W. Holloway, 117 W. Duval St., Jacksonville, Fla.
Place: Birmingham, Ala. Time: November 16-18, 1932.

STATE

Alabama Pediatric Society

President: Dr. Thomas J. McElhenney, 1722, 2nd Ave., Bessemer.
Secretary-Treasurer: Dr. John W. Simpson, 1117 S. 22nd St., Birmingham.
Place: Mobile. Time: April 19-21, 1932.

Georgia Pediatric Society

President: Dr. Charles E. Boynton, 118 Forrest Ave., N. E., Atlanta.
Secretary-Treasurer: Dr. Roger W. Dickson, 33 Ponce de Leon Ave., N. E., Atlanta.

Louisiana State Pediatric Society

President: Dr. R. T. Lucas, Shreveport, La.
Secretary-Treasurer: Dr. Suzanne Schaeffer, Chailie Bldg., New Orleans.

Medical Society of State of New York

Chairman: Dr. Albert D. Kaiser, 16 N. Goodman St., Rochester.
Secretary: Dr. Adolph G. G. De Sanctis, 12 E. 11th St., New York.
Place: Buffalo. Time: May, 1932.

Nebraska Pediatric Society

President: Dr. H. B. Hamilton, 434 Aquila Court Bldg., Omaha.
Secretary: Dr. George L. Clark, 1817 Vinton St., Omaha.
Place: As announced by committee. Time: Second Thursday of each month from October to June, inclusive, 6 p. m.

Oklahoma State Pediatric Society

President: Dr. C. E. Bradley, Medical Arts Bldg., Tulsa.
Secretary: Dr. G. H. Harrison, 1200 N. Walker St., Oklahoma City.
Place: Tulsa. Time: May 14, 1932.

South Carolina Pediatric Society

President: Dr. E. W. Barron, 1512 Marion St., Columbia.
Secretary-Treasurer: Dr. Julian P. Price, 117 W. Cheves St., Florence.

Texas Pediatric Society

President: Dr. J. H. Park, Jr., 3717 Main St., Houston.
Secretary-Treasurer: Dr. P. E. Luecke, 4105 Live Oak St., Dallas.

Virginia Pediatric Society

President: Dr. St. Geo. Grinnan, 925 W. Grace St., Richmond.
Secretary-Treasurer: Dr. J. B. Stone, 2042 Park Ave., Richmond.

LOCAL

Academy of Medicine of Cleveland, Pediatric Section

Chairman: Dr. J. E. McClelland, 10515 Carnegie Ave., Cleveland.
Secretary: Dr. P. G. Albrecht, 2009 Adelbert Rd., Cleveland.
Place: 2009 Adelbert Road. Time: Four meetings, from September to May.

Academy of Medicine, Toronto, Section of Pediatrics

President: Dr. Gladys Boyd, 56 DeLisle St., Toronto.
Secretary: Dr. Lawrence Murray, 1870 Bloor St., W., Toronto.

Bronx Pediatric Society

President: Dr. Joseph Golomb, 496 E. 17th St., New York.
Secretary: Dr. E. Leonard Benjamin, 2229 Valentine Ave., New York.
Place: Concourse Plaza, 161st St. and Grand Concourse. Time: Second Wednesday of each month, except June, July, August and September.

Brooklyn Pediatric Society

President: Dr. Irwin Schiff, 658 Eastern Parkway, Brooklyn.
Secretary: Dr. Louis A. Koch, 62 Pierrepont St., Brooklyn.
Place: Kings County Medical Society Bldg. Time: Last Wednesday of each month, except June, July and August.

Central New York Pediatric Club

President: Dr. Frank Vander Bogert, 111 Union St., Schenectady.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Place: Various cities in New York. Time: Fourth Thursday of October, January and April.

Chicago Pediatric Society

President: Dr. Henry E. Irish, 432 S. Lincoln St., Chicago.
Secretary: Dr. Bert I. Beverly, 8 S. Michigan Ave., Chicago.
Place: City Club. Time: Third Tuesday of each month.

Dallas County Pediatric Society

President: Dr. Gordon B. McFarland, Medical Arts Bldg., Dallas, Texas.
Secretary: Dr. Harold T. Nesbit, Medical Arts Bldg., Dallas, Texas.
Place: Bradford Memorial Hospital. Time: 1 p. m., first and third Saturdays of each month.

Detroit Pediatric Society

President: Dr. Charles Wilson, 10 Peterboro St., Detroit.
Secretary: Dr. Joseph A. Johnston, Henry Ford Hospital, Detroit.
Place: Children's Hospital of Michigan. Time: No fixed date; approximately once a month.

Fulton County Medical Society, Pediatric Section (Atlanta, Ga.)

Chairman: Dr. James A. Wood, Medical Arts Bldg., Atlanta.
Secretary: Dr. Roger W. Dickson, 33 Ponce de Leon Ave., N. E., Atlanta.
Place: Academy of Medicine, 32 Howard St. Time: Second Thursday of each month from October to April, 8 p. m.

Memphis Pediatric Society

President: Dr. William R. Graves, 1193 Madison Ave., Memphis, Tenn.
Secretary-Treasurer: Dr. Harry J. Jacobson, 1193 Madison Ave., Memphis, Tenn.
Place: Memphis General Hospital. Time: Second Tuesday of each month.

Milwaukee Pediatric Society

President: Dr. G. H. Fellman, 231 W. Wisconsin Ave., Milwaukee.
Secretary: Dr. George F. Kelly, 161 W. Wisconsin Ave., Milwaukee.
Place: Children's Hospital. Time: Second Wednesday of each alternate month, beginning with February.

New England Pediatric Society

President: Dr. Lewis Webb Hill, 319 Longwood Ave., Boston.
Secretary: Dr. Gerald Hoeffel, 319 Longwood Ave., Boston.
Place: Boston Medical Library. Time: Four meetings a year, occurring from September to May.

New York Academy of Medicine, Section of Pediatrics

Chairman: Dr. Herbert B. Wilcox, 39 E. 75th St., New York.
Secretary: Dr. John Caffey, 50 Haven Ave., New York.
Place: New York Academy of Medicine, 2 E. 103d St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

Northern California Pediatric Society

President: Dr. Edward B. Shaw, 384 Post St., San Francisco.
Secretary-Treasurer: Dr. Lloyd Hardgrave, 384 Post St., San Francisco.
Place: Various teaching schools. Time: Monthly.

Northwestern Pediatric Society

President: Dr. E. S. Platou, Medical Arts Bldg., Minneapolis.
Secretary: Dr. F. G. Hedenstrom, 625 Lowry Bldg., St. Paul.

Philadelhia Pediatric Society

President: Dr. John P. Scott, 2040 Pine St., Philadelphia.
Secretary: Dr. John D. Donnelly, 115 Bryn Mawr Ave., Bala, Pa.
Place: College of Physicians, 19 S. 22d St. Time: Second Tuesday of each month from October to June, inclusive.

Pittsburgh Pediatric Society

President: Dr. David H. Boyd, 200, 9th St., Pittsburgh.
Secretary: Dr. Theodore O. Elterich, 724 Highland Bldg., Pittsburgh.
Place: Pittsburgh Academy of Medicine. Time: Second Friday, alternate months from October to April, inclusive.

Richmond Pediatric Society

President: Dr. Henry S. Stern, 807 W. Franklin St., Richmond, Va.
Secretary-Treasurer: Dr. W. C. Chapin, 922 Floyd Ave., Richmond, Va.
Place: Westmoreland Club, 601 E. Grace St. Time: First Thursday of each month (other than during the summer).

Rochester Pediatric Society

President: Dr. S. W. Clausen, Strong Memorial Hospital, Rochester, N. Y.
Secretary: Dr. F. W. Bush, 221 S. Goodman St., Rochester, N. Y.
Place: Arranged by program committee. Time: First Friday of each month from October to May.

Rocky Mountain Pediatric Society

President: Dr. Wilford W. Barber, 227, 16th St., Denver.
Secretary: Dr. John A. Schoonover, 1616 Tremont Pl., Denver.
Place: Children's Hospital, Denver. Time: Third Saturday of each month from September to May, inclusive, 2:30 p. m.

St. Louis Pediatric Society

President: Dr. Gustave Lippmann, 3720 Washington Blvd., St. Louis.
Secretary-Treasurer: Dr. Katherine Bain, 3720 Washington Blvd., St. Louis.
Place: St. Louis Medical Society. Time: Third Friday of every month.

Seattle Pediatric Society

President: Dr. C. L. Smith, 1215, 4th Ave., Seattle.
Secretary: Dr. N. W. Murphy, 515 Cobb Bldg., Seattle.
Place: College Club. Time: Third Friday of each month, 7 p. m.

Southwestern Pediatric Society

President: Dr. William M. Happ, 523 W. 6th St., Los Angeles.
Secretary: Dr. Jeanette Harrison, 1136 W. 6th St., Los Angeles.
Place: University Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

University of Michigan Pediatric and Infectious Disease Society

President: Dr. Henry G. Poncher, 5325 Kenmore Ave., Chicago.
Secretary: Dr. John P. Parsons, 320 S. Division St., Ann Arbor, Mich.
Place: Ann Arbor, Mich. Time: November, 1932.

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